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(57) Abstract

This invention is the coadministration of ACAT and MMP inhibitors for the reduction of both the macrophage and smooth muscle cell component of atherosclerotic lesions, thus impairing the expansion of existing lesions and the development of new lesions and for the prevention of plaque rupture and the promotion of lesion regression in a mammal.

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COADMINISTRATION OF ACAT AND MMP INHIBITORS FOR THE TREATMENT OF ATHEROSCLEROTIC LESIONS

BACKGROUND OF THE INVENTION

Enzymes known as native matrix metalloproteinases (MMP) are classes of naturally occurring enzymes found in most mammals. They are zinc proteases that hydrolyze collagens, proteoglycans, and glycoproteins. The classes include gelatinase A and B, stromelysin-1 and -2, fibroblast collagenase, neutrophil collagenase, matrilysin, metalloelastase, and interstitial collagenase. These enzymes are implicated in a number of diseases which result from breakdown of connective tissues, such as rheumatoid arthritis, osteoarthritis, osteoporosis, multiple sclerosis, and even tumor metastasis. The expression of MMPs in atherosclerosis is discussed in White A., Bocan T.M.A., Boxer P.A., Peterson J.T., Schrier D. Emerging therapeutic advances for the development of second generation matrix metalloproteinase inhibitors. *Curr. Pharm. Design* 3:45-58 (1997). To date, inhibitors of matrix metalloproteinases have not been utilized with ACAT inhibitors.

United States Patent Application 08/987167 filed December 8, 1997, teaches MMP inhibitors and their preparation and is hereby incorporated by reference.

Compounds which inhibit acyl-coenzyme A:cholesterol acyltransferase are known as ACAT inhibitors. Certain ACAT inhibitors and the methods for preparing them are taught in United States Patent 5,491,172 and its divisional 5,633,287 which are hereby incorporated by reference.

United States Patent 5,756,545 covers MMP inhibitors especially 2-(4′-Bromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid. This patent is hereby incorporated by reference.

United States Patent 5,441,975 teaches ACAT inhibitors, especially N-(2,6-Diisopropyl-phenyl)-2-(2-dodecyl-2H-tetrazol-5-yl)-2-phenyl-acetamide. This and other patents in the same patent family: 5,646,170; 5,693,657; and 5,366,987 are hereby incorporated by reference.

SUMMARY OF THE INVENTION

The instant invention is the coadministration of ACAT and MMP inhibitors for the reduction of both macrophage and smooth muscle cell components of atherosclerotic lesions in a mammal, particularly a human. The lesions are directly reduced, and so, the expansion of existing lesions and the development of new ones is impaired.

Certain ACAT inhibitors and certain MMP inhibitors are disclosed as suitable for coadministration.

Pharmaceutical compositions of the inhibitors are also included in the invention.

DETAILED DESCRIPTION OF THE INVENTION

Coadministration of a bioavailable ACAT inhibitor with a matrix metalloproteinase (MMP) inhibitor can blunt the development of atherosclerotic lesions and promote development of a stable plaque morphology. ACAT inhibitors have been shown to reduce the accumulation of monocyte-macrophages within atherosclerotic lesions of rabbits. In addition, monocyte-macrophages have been reported to secrete such matrix metalloproteinases as MMP-7 and -9 while smooth muscle cells are noted to secrete MMP-1, -2, and -3. Inhibition of ACAT while directly reducing the accumulation of lipid-filled monocyte-macrophages will decrease the source of MMPs. Inhibition of MMPs will also limit the development of atherosclerotic lesions through reducing smooth muscle cell and monocyte migration into the development intima by limiting extracellular matrix remodeling. Coadministration of both agents will limit the development of new lesions by inhibiting cellular accumulation and stabilize the developed lesions by preventing both matrix remodeling and reducing the number of lipid-filled monocyte-macrophages, a source of MMP-7 and -9.

The instant invention is a method for treating and/or preventing atherosclerotic lesions comprising coadministrating one or more MMP inhibitors and one or more ACAT inhibitors.

The invention is further a method for preventing plaque rupture and for promoting lesion regression by administering a combination of an ACAT inhibitor and an MMP inhibitor.

The method is practiced by administering a chemical compound effective in inhibiting the biological activity of a matrix metalloproteinase such as collagenase, stromelysin, gelatinase, or elastase. The numerous compounds known to be matrix metalloproteinase inhibitors are useful in the practice of this invention.

The method is practiced by administering a chemical compound which inhibits the enzyme acyl-coenzyme A:cholesterol acyltransferase. The numerous compounds known as ACAT inhibitors are useful in the practice of this invention.

A "matrix metalloproteinase inhibitor" as used herein is any chemical compound that inhibits by at least five percent the hydrolytic activity of at least one matrix metalloproteinase enzyme that is naturally occurring in a mammal. Such compounds are also referred to as "MMP inhibitors." Numerous matrix metalloproteinase inhibitors are known, and all are useful in the method of this invention. For example, 4-biarylbutyric and 5-biarylpentanoic acid derivatives are described in United States Patent Application 339846 filed November 15, 1994, which is incorporated herein by reference. The compounds are defined generally as $(T)_XA$-B-D-E-G. Over 400 specific compounds are named, and each is incorporated herein and can be employed in this invention. Especially preferred compounds to be utilized include the following:

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-(2-methylpropyl)-γ-oxo-, (*S*)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-(2-methylpropyl)-γ-oxo-, (*R*)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-β-(2-methylpropyl)-γ-oxo-, (*S*);

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-β-(2-methylpropyl)-γ-oxo-, (*R*)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-bromo-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-fluoro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-fluoro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′,4′-difluoro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 3′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-(2-methyl-propyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-bromo-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-fluoro-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-ethyl-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-fluoro-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-chloro-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-methoxy-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′,4′-difluoro-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-methyl-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-(2-methyl-propyl)-γ-oxo-4′-pentyl-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-methylene-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-chloro-α-methylene-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-methyl-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-pentyl-;

Benzenebutanoic acid, 4-chloro-α-(2-methylpropyl)-γ-oxo-;

Benzenebutanoic acid, 4-methyl-α-methylene-γ-oxo-;

2-Butenoic acid, 4-(4′-chloro[1,1′-biphenyl]-4-yl)-4-oxo-, (*E*)-;

2-Butenoic acid, 4-[4-(4-chlorophenyoxy)-phenyl]-4-oxo, (*E*)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-hydroxy-α-(2-methylpropyl)-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-β-methylene-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-hydroxy-α-(2-methylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-hydroxy-α-(2-methylpropyl)-;

2(3H)-Furanone, 5-(4′-chloro[1,1′-biphenyl]-4-yl)dihydro-3-(2-methylpropyl)-;

2(3H)-Furanone, 5-(4′-chloro[1,1′-biphenyl]-4-yl)dihydro-3-(2-methylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 3′,4′-dichloro-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 3′,5′-dichloro-γ-oxo-α-(3-phenylpropyl)-;

[1,1′–Biphenyl]-4-butanoic acid, 4′-(acetyloxy)-γ-oxo-α-(3-phenylpropyl)-;

Benzenepentanoic acid, α-[2-[4-(5-chloro-2-thienyl)phenyl]-2-oxoethyl]-;

2-Furancarboxylic acid, 5-[4-(3-carboxy-1-oxo-6-phenylhexyl)phenyl]-;

Benzenepentanoic acid, α-[2-oxo-2-[4-(3-pyridinyl)phenyl]ethyl]-;

Benzenepentanoic acid, α-[2-oxo-2-[4-[6-(pentyloxy)-3-pyridinyl]-phenyl]ethyl]-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(pentylthio)-α-(3-phenylpropyl) ;

[1,1′-Biphenyl]-4-butanoic acid, 4′-methoxy-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 3′-chloro-4′-fluoro-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-ethoxy-γ-oxo-α-(3-phenylpropyl)-;

Benzenepentanoic acid, α-[2-oxo-2-[4-(3-thienyl)phenyl]ethyl]-;

[1,1′-Biphenyl]-4-butanoic acid, 2′,4′-dichloro-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-formyl-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(3-phenylpropyl)-3′,5′-bis(trifluoromethyl)-;

Benzenepentanoic acid, α-[2-oxo-2-[4-(2-thienyl)phenyl]ethyl]-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(3-phenylpropyl)-3′-(trifluoromethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 2′-formyl-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4-hydroxy-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(3-phenylpropyl)-4′-propoxy-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(pentyloxy)-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(pentyloxy)-α-(3-phenylpropyl)-, (S)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(pentyloxy)-α-(3-phenylpropyl)-, (R)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(hexyloxy)-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-butoxy-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(3-phenylpropoxy)-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(1-methylethoxy)-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(heptyloxy)-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(cyclohexyl-methoxy)-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(2-methyl-propoxy)-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(3-phenylpropyl)-4′-(2-propenyloxy)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-heptyl-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-decyl-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-nitro-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-cyano-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(2-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(3-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(4-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(3,5-dimethoxyphenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-phenyl-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-(phenylmethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-[(trimethylsilyl)-methyl]-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-bromo-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, -γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-amino-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(2-phenylethyl)-4′-[[(phenylmethoxy)carbonyl]amino]-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-[[(1,1-dimethylethoxy)-carbonyl]amino]-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(acetylamino) γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-[(1-oxopentyl)amino]-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-[(3,3-dimethyl-1-oxobutyl)amino]-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[2-(methoxycarbonyl)-phenyl]ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(2-carboxyphenyl)ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[2-[(diethylamino)-carbonyl]phenyl]ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[3-[(diethylamino)carbonyl]phenyl]ethyl]-γ-oxo-, (*S*)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[3-[(diethylamino)carbonyl]phenyl]ethyl]-γ-oxo-, (*R*)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(phenylmethoxy)methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-(phenoxymethyl)-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(benzoyloxy)-methyl]-5-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, (1α,2β,5β)-;

1,2-Benzenedicarboxylic acid, 1-[[2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]-methyl]-2-methyl ester,(1α,2β,3α)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(2-thienylthio)methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(benzoylamino)methyl]-5-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[[(2-methoxyethoxy)methoxy]methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[[(phenylmethyl)thio]methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(phenylthio)methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(propylthio)methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(2-benzothiazolylthio)methyl]-5-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, (1α,2β,5β)-;

Benzoic acid, 2-[[[2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl]thio]-, 1-methyl ester, (1α,2β,3α)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[[[(phenylmethoxy)carbonyl]-amino]methyl]-, (1α,2β,5β)-;

Benzoic acid, 2-methyl-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Benzoic acid, 3-methyl-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Benzoic acid, 4-methyl-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Benzoic acid, 2-methoxy-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Benzoic acid, 3-methoxy-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Benzoic acid, 4-methoxy-, [2-carboxy-3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]cyclopentyl]methyl ester, (1α,2β,3α)-;

Cyclopentanecarboxylic acid, 2-[(2-benzoxazolylthio)methyl]-5-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-4-nitro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-, (1α,2β,5β)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(1,3-dihydro-5-nitro-1,3-dioxo-2*H*-isoindol-2-yl)methyl]-, (1α,2β,5β)-;

2*H*-Benz[*f*]isoindole-2-butanoic acid, α-[2-(4′-ethoxy[1,1′-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-(acetylamino)-4′-chloro-γ-oxo-;

2*H*-Isoindole-2-hexanoic acid, α-[2-(4′-chloro[1,1′-biphenyl]-4-yl)-2-oxoethyl]-1,3-dihydro-1,3-dioxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[[[3-(methoxycarbonyl)-phenyl]thio]methyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[[(2,6-(dimethylphenyl)-thio]methyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[[[4-fluoro-2-(methoxycarbonyl)phenyl]thio]methyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[[[3-[(diethylamino)-carbonyl]phenyl]thio]methyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[[[2-[(dimethylamino)-carbonyl]phenyl]thio]methyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4'-chloro-α-[[[3-[(dimethylamino)-carbonyl]phenyl]thio]methyl-]-γ-oxo-;

Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid, 3-[[4′-(pentyloxy)[1,1′-biphenyl]-4-yl]carbonyl]-, (2-*endo*,3-*exo*)-;

1-Cyclopentene-1-carboxylic acid, 5-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-5-[(phenylmethyl)thio]-, (1α,2β,5α)-;

Cyclopentanecarboxylic acid, 2-[(4′-chloro[1,1′-biphenyl-4-yl)carbonyl]-5-[(phenylmethyl)thio]-, (1α,2β,5β)-;

1-Cyclopentene-1-carboxylic acid, 5-[[4′-(pentyloxy)[1,1′-biphenyl]-4-yl]carbonyl]-;

1-Cyclopentene-1-carboxylic acid, 5-[[4′-(hexyloxy)[1,1′-biphenyl]-4-yl)]carbonyl]-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-hydroxy-γ-oxo-α-[(phenylthio)-methyl]-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-[2-[(butylamino)-carbonyl]phenyl]ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(3-carboxyphenyl)ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[3-[(diethylamino)-carbonyl]phenyl]ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-[3-[(butylamino)carbonyl]-phenyl]ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[4-[(diethylamino)-carbonyl]phenyl]ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-[4-[(butylamino)-carbonyl]phenyl]ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(4-carboxyphenyl)ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-methoxy-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-hydroxy-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-ethoxy-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(2-phenylethyl)-4′-propoxy-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-(pentyloxy)-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(hexyloxy)-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-butoxy-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(2-phenylethyl)-4′-(phenylmethoxy)-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(3-iodophenyl)ethyl]-γ-oxo-4′-(pentyloxy)-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(3-iodophenyl)ethyl]-γ-oxo-4′-(phenylmethoxy)-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(3-[(diethylamino)carbonyl]-phenyl]ethyl]-γ-oxo-4′-(pentyloxy)-;

[1,1′-Biphenyl]-4-butanoic acid, α-[2-(3-[(diethylamino)carbonyl]-phenyl]ethyl]-γ-oxo-4′-(phenylmethoxy)-;

1,2-Pyrrolidinedicarboxylic acid, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, 1-(phenylmethyl) ester, (2*S-trans*)-;

1,2-Pyrrolidinedicarboxylic acid, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-, 1-(phenylmethyl) ester, (2′*R-trans*)-;

L-Proline, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-1-[[(phenylmethyl)amino]carbonyl]-, *trans*-;

L-Proline, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-1-(1-oxo-3-phenylpropyl)-, *trans*-;

L-Proline, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-1-(phenylacetyl)-, *trans*-;

L-Proline, 3-[(4′-chloro[1,1′-biphenyl]-4-yl)carbonyl]-1-(3,3-dimethyl-1-oxobutyl)-, *trans*-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-heptyl-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-decyl-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-nitro-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-cyano-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(2-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(3-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(4-iodophenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-(3,5-dimethoxyphenyl)ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-phenyl-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-(phenylmethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-γ-oxo-α-[(trimethylsilyl)-methyl]-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-bromo-γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(3-phenylpropyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-amino-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-α-(2-phenylethyl)-4′-[[(phenylmethoxy)carbonyl]amino]-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-[[(1,1-dimethylethoxy)-carbonyl]amino]-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-(acetylamino)-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, γ-oxo-4′-[(1-oxopentyl)amino]-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-[(3,3-dimethyl-1-oxobutyl)amino]-γ-oxo-α-(2-phenylethyl)-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[2-methoxycarbonyl)-phenyl]ethyl]-γ-oxo-;

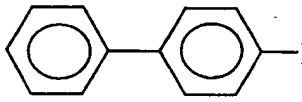
[1,1′-Biphenyl]-4-butanoic acid, α-[2-(2-carboxyphenyl)ethyl]-4′-chloro-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[2-[(diethylamino)-carbonyl)phenyl]ethyl]-γ-oxo-;

[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[3-[(diethylamino)-carbonyl)phenyl]ethyl]-γ-oxo-, (*S*)-; and

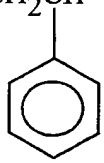
[1,1′-Biphenyl]-4-butanoic acid, 4′-chloro-α-[2-[3-[(diethylamino)-carbonyl)phenyl]ethyl]-γ-oxo-, (*R*)-.

Fenbufen and compounds related to fenbufen can be utilized. Such compounds are described in United States Patent Number 3,784,701 and by Child, et al., *J. Pharm. Sci.*, 1977;66:466-476, and Arzneim-Forsch, 1980;30(4A):695-702, all of which are incorporated herein by reference. Preferred compounds from the fenbufen series to be utilized in this invention have the formula

 , where R is

CCH_2CH_2COOH (fenbufen), $COCH{=}CHCOOH$, SO_2NH_2, $COCH_2CHCOOH$,
|
CH_3

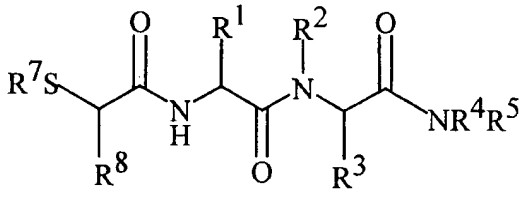
$COCH_2CH$—$COOH$

 , $COCH_2CH_2SO_3Na$, $CH(OH)CH_2CH_2COOH$,

$COCH_2CHCOOH$, $COCH_2CH_2CONHOH$, $C(=NOH)CH_2CH_2COOH$, and
|
OH

$COCH_2SCH_2COOH$.

Numerous peptides are known matrix metalloproteinase inhibitors. Typical of such peptides are those described in United States Patent Number 5,300,501; 5,530,128; 5,455,258; 5,552,419; WO 95/13289; and WO 96/11209, all of which are incorporated herein by reference. Such compounds are illustrated by the formula



where each of the variable groups can include hydrogen alkyl, aryl, heteroaryl, alkenyl, alkynyl, carboxy, and the like. Preferred compounds from within this class which can be utilized in the method of this invention include the following:

N-[2,3-bis-Acetylmercaptopropanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-3-methoxycarbonylpropanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-4-methoxycarbonylbutanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-5-methoxycarbonylpentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-4-phthalimidobutanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-phthalimidohexanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2,3-*bis*-Mercaptopropanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-3-methoxycarbonylpropanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-4-methoxycarbonylbutanyol]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-4-methoxycarbonylpentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-4-phthalimidobutanoyl]-L-leucyl-phenyl-alanine N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-6-phthalimidohexanyoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-5-methoxycarbonylpentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanyol]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanyol]-L-valinyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanyol]-L-leucyl-L-tryptophan N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-valinyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-L-tryptophan N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-L-[β-(4-thiazolyl)]alaine N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-L-(β-(2-pyridyl)alanine N-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-L-leucyl-5-methyl-L-glutamicacid N-methylamide;

N-[2-Acetylmercapto-6-phthalimidohexanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Acetylmercapto-2-(3-phthalimido) phenylacetyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-5-methoxycarbonylpentanoyl]-L-phenylalanine N-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanyol]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanyol]-L-leucyl-L-trptophan N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-L-tryptophan N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-L-[β-(4-thiazolyl)alanine N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-L-[β-(2-pyridyl)]alanine N-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-L-leucyl-5-methyl-L-glutamic acid N-methylamide;

N-[2-Mercapto-6-phthalimidohexanoyl]-L-leucyl-L-phenylalanine N-methylamide;

N-[N-Mercaptoacetyl)-L-leucyl]-L-phenylalanine N-methylamide;

N-[Acetomercaptoacyl)-L-leucyl-L-phenylalanine methylamide;

(RS)-2-(Acetylthio)pentanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)propanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-3-methylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-2-phenylacetyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-3-phenylpropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-4-phenylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

N-(Acetylmercaptoacyl)-L-threonyl-L-phenylalanine methylamide;

N-(Acetylmercaptoacyl)-L-leucyl-L-tryptophan methylamide;

(RS)-2-Mercaptopentanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercaptopropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-3-methylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-2-phenylacetyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-3-phenylpropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-4-phenylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

N-[N-(Mercaptoacetyl)-L-threonyl]-L-phenylalanine methylamide;

N-[N-(Mercaptoacetyl)-L-leucyl]-L-tryptophan methylamide;

[4-(N-Hydroxyamino)-2(R)-cyclohexylmethylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-N-(Hydroxyamino)-2R-isobutylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-(N-hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-[2-(N,N-dimethylamino]ethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-[2-(p-sulphonamidophenyl)ethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-(2-(p-sulphonylphenyl)ethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-[2-(2-pyridyl)ethyl]amide;

[4-(N-Hydroxyamino)-2R-pentylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2R-isoamylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylbutylsuccinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-[3-(4-morpholinyl)propyl]amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-β-cyclohexylalanine-N-[β-alanine]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-β-cyclohexylalanine amide;

[4-(N-Hydroxyamino)-2R-(3-phenylpropyl)succinyl]-L-β-cyclohexylalanine amide;

[4-(N-Hydroxyamino)-2R-(3-phenylbutyl)succinyl]-L-β-cyclohexylalanine amide;

[4-N-(Hydroxyamino)-2R-phenylethylsuccinyl]-L-leucine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2R-phenylpropylsuccinyl]-L-leucine-N-(2-phenylethyl)amide;

[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-L-tryptophan amide;

[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-L-valine amide;

[3-Phosphono-2R,S-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide, dimethylester;

[3-Phosphono-2R-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

[3-Phosphono-2S-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine-β-alanine;

[3-Phosphono-2R-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine;

[3-Phosphono-2S-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine-β-alanine, methyl ester;

[3-Phosphono-2R,S-phenylpropyl-1-oxopropyl]-L-β-cyclohexylalanine-N-[4(3-aminopropyl)morpholine]amide, bromine salt;

[3-Phosphono-2R,S-(4-methylphenyl)propyl-1-oxopropyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide, diethylester;

[3-Phosphono-2R,S-(4-methylphenyl)propyl-1-oxopropyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)-amide;

4-t-Butoxy-2(R)-[3-(2-phenoxyethyl)succinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

4-Hydroxy-2(R)-[3-(2-phenoxyethyl)succinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

4-(N-Hydroxyamino-2(R)-[3-(2-phenoxyethyl)succinyl]-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

{4-Hydroxy-2(R)-[3-(4-pyridinium)propyl]succinyl}-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

{4-(N-Hydroxyamino)-2(R)-[3-(4-pyridinium)propyl]succinyl}-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

{4-(N-Hydroxyamino)-2(R)-[3-(N-methyl-4-pyridinium)propyl]succinyl}-L-β-cyclohexylalanine-N-(2-phenylethyl)amide;

{4-Hydroxy-2-(R)-[3-(4-methylphenyl)propyl]succinyl}-L-β-cyclohexylalanine-N-[(2-morpholine-sulphonylamino)ethyl]amide;

{4-(N-Hydroxyamino)-2-(R)-[3-(4-methylphenyl)propyl]succinyl}-L-β-cyclohexylalanine-N-[(2-morpholinesulphonylamino)ethyl]amide;

{4-(N-Hydroxyamino)-2-(R)-[3-(4-chlorophenyl)propyl]succinyl}-L-β-cyclohexylalanine-N-[(2-morpholinesulphonylamino)ethyl]amide;

{4-N-Hydroxyamino)-2-(R)-[3-(4-methylphenyl)propyl]succinyl}-L-β-cyclohexylalanine-N-[(2-dimethylsulphonylamino)propyl]amide;

[4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl]-L-[S-(methyl)penicillamine]-N-methylamide;

[4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl]-L-[S-(methyl)penicillamine]amide;

[4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl]-L-penicillamine]amide;

{4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl}-L-[S-(methyl)penicillaminesulphone]-N-methylamide;

{4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl}-L-[S-(methyl)penicillaminesulphoxide]-N-methylamide;

{4-(N-Hydroxyamino)-2(R)-[3-(4-chlorophenyl)propyl]succinyl}-L-penicillamine-N-methylamide;

[4-(N-Hydroxyamino)-2(R)-3-(2-methylpropyl)succinyl]-L-[S-methyl)penicillamine]-N-methylamide;

N^4-Hydroxy-N^1-(1-(S)-carbamoyl-2,2-dimethylpropyl)-2-(R)-4-(chlorophenylpropyl)succinamide;

N^4-Hydroxy-N^1-(1-(S)-carbamoyl-2,2-dimethylpropyl)-2-(R)-(4-methylphenylpropyl)succinamide;

N^4-Hydroxy-N^1-(1-(S)-carbamoyl-2,2-dimethylpropyl)-2-(R)-(4-methoxyphenylpropyl)succinamide;

N^4-Hydroxy-N^1-(1-(S)-carbamoyl-2,2-dimethylpropyl)-2-(R)-(4-trifluoromethylphenylpropyl)succinamide;

N^4-Hydroxy-N^1-(1-(S)-carbamoyl-2,2-dimethylpropyl)-2-(R)-(4-chloromethylphenylpropyl)succinamide;

N-[N-(Mercaptoacetyl)-L-leucyl]-L-phenylalanine methylamide;

N-(Acetomercaptoacyl)-L-leucyl]-L-phenylalanine methylamide;

(RS)-2-(Acetylthio)pentanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)propanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-3-methylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-2-phenylacetyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-3-phenylpropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-(Acetylthio)-4-phenylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

N-(Acetylmercaptoacyl)-L-threonyl-L-phenylalanine methylamide;

N-(Acetylmercaptoacyl)-L-leucyl-L-tryptophan methylamide;

(RS)-2-Mercaptopentanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercaptopropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-3-methylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-2-phenylacetyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-3-phenylpropanoyl-L-leucyl-L-phenylalanine N-methylamide;

(RS)-2-Mercapto-4-phenylbutanoyl-L-leucyl-L-phenylalanine N-methylamide;

N-[N-(Mercaptoacetyl)-L-threonyl]-L-phenylalanine methylamide;

N-[N-(Mercaptoacetyl)-L-leucyl]-L-tryptophan methylamide;

N-[2,3-*bis*-Acetylmercaptopropanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-3-methoxycarbonylpropanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-4-methoxycarbonylbutanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-5-methoxycarbonylpentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-4-phthalimidobutanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-6-phthalimidohexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2,3-*bis*-Mercaptopropanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-3-methoxycarbonylpropanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-4-methoxycarbonylbutanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-5-methoxycarbonylpentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-4-phthalimidobutanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-6-phthalimidohexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-5-methoxycarbonylpentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanoyl]-*L*-valinyl-*L*-phenylalanine N-methylamide;

N-[2-Acetylmercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-tryptophan *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-valinyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-tryptophan *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-[β-(4-thiazolyl)]alanine *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-[β-(2-pyridyl)]alanine *N*-methylamide;

N-[2-Acetylmercapto-5-phthalimidopentanoyl]-*L*-leucyl-5-methyl-*L*-glutamic acid *N*-methylamide;

N-[2-Acetylmercapto-6-phthalimidohexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Acetylmercapto-2-(3-phthalimido)phenylacetyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-5-methoxycarbonylpentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-6-methoxycarbonylhexanoyl]-*L*-leucyl-*L*-tryptophan *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-tryptophan *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-[β-(4-thiazolyl)alanine *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-*L*-[β-(2-pyridyl)]alanine *N*-methylamide;

N-[2-Mercapto-5-phthalimidopentanoyl]-*L*-leucyl-5-methyl-*L*-glutamic acid *N*-methylamide;

N-[2-Mercapto-6-phthalimidohexanoyl]-*L*-leucyl-*L*-phenylalanine *N*-methylamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(3-picolyl)amino]-3-methylbutanamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-3-picolyl)amino]-2-cyclohexylacetamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(benzyl)amino]-4-methylpentanamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(benzyl)amino]-6-[(N,N-dimethylglycyl)amino]hexanamide hydrochloride;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(3-picolyl)amino]-3-methylbutanamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(4-picolyl)amino]-2-cyclohexylacetamide;

N-Hydroxy-2(R)-[(4-methoxybenzenesulfonyl]-(4-picolyl)amino]-2-(2-tetrahydrofuranyl)acetamide;

N-Hydroxy-2(R)-[[4-methoxybenzenesulfonyl]-(3-picolyl)amino]-3-methylbutanamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-benzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methoxyphenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methoxybenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-thiophenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-thiobenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(methylthio-2-thienyl)succinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylacetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-isopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-thioacetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-thioisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-(2-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-(3-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-(4-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl thio-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-benzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methoxyphenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methoxybenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylthiophenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylthiobenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-(methylthio-2-thienyl)succinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-benzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methyl acetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methyl tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylthioacetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylthioisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methylthio-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methyl-(2-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methyl-(3-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-hexyl-3S-methyl-(4-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-benzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methoxyphenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methoxybenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylthiophenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylthiobenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-(methylthio-2-thienyl)-succinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-benzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methyl acetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methyl-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylthioacetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylthioisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-ethylphenyl-3S-methylthio-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthiophenylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthiobenzylsuccinyl]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthio-2-thienyl)succinyl]-N^1-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methyl acetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methyl tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthioacetate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthioisopropanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methylthio-tert-butanoate]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methyl-(2-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methyl-(3-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-octyl-3S-methyl-(4-pyridyl)]-N^2-(S)-piperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-N^2-(S)-4′(S/R)-benzylpiperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-N^2-(S)-5′(S/R)-benzylpiperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-N^2-(S)-6′(S/R)-benzylpiperazic acid N-methyl amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-N^2-S)-[5′,6′]benzopiperazic acid N-methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-isobutylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-hexylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-heptylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-octylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-ethylphenylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-propylphenylclycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethylthiobenzyl]-α-(S)-isobutylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethylthiobenzyl]-α-(S)-hexylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethylthiobenzyl]-α-(S)-ethylphenylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethylthiobenzyl]-α-(S)-propylphenylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyloxybenzyl]-α-(S)-isobutylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyloxybenzyl]-α-(S)-hexylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyloxybenzyl]-α-(S)-ethylphenylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-ethyloxybenzyl]-α-(S)-propylphenylglycine-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxy-4-(p-toluenesulfonyl)butyl]-α-(S)-phenethylglycyl-(S)-N^2-piperazic acid methyl amide;

N-[1(R)-Carboxyethyl]-α-[2-(4-phenylphenoxy)ethyl]-glycyl-(S)-N^2-piperazic acid methyl amide;

2-[2(R)-[2-[1,1′-Biphenyl)yl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[1,1′-Biphenyl)yl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[1,1′-Biphenyl)yl]propyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-(4-Propylphenyl)ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-(4-Butylphenyl)ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-(4-t-Butylphenyl)ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(4-Fluorophenyl)phenyl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(4-Fluorophenyl)phenyl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-n-Octyl-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Thiazolyl)phenyl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Thiazolyl)phenyl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Thiazolyl)phenyl]ethyl]-4-[3-(phenylsulfonyl)propyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Thiazolyl)phenyl]ethyl]-4-(3-phenylpropyl)-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Oxazolyl)phenyl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Oxazolyl)phenyl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Oxazolyl)phenyl]ethyl]-4-[3-(phenylsulfonyl)propyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Oxazolyl)phenyl]ethyl]-4-(3-phenylpropyl)-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(Dimethylamino)methylphenyl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(Dimethylamino)methylphenyl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(Dimethylamino)methylphenyl]ethyl]-4-[3-(phenylsulfonyl)propyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[4-(Dimethylamino)methylphenyl]ethyl]-4-(3-phenylpropyl)-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Imidazolyl)phenyl]ethyl]-4-butyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Imidazolyl)phenyl]ethyl]-4-methyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Imidazolyl)phenyl]ethyl]-4-[3-(phenylsulfonyl)propyl-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

2-[2(R)-[2-[(4-Imidazolyl)phenyl]ethyl]-4-[3-(phenylpropyl)-4(S)-carboxy-1-oxobutyl]-3(S)-methylaminocarbonyl-hexahydropyridazine;

$HS(CH_2)_2$-(S-*D*-Leu)-Phe-NHMe;

HS(*S*)$CHMeCH_2$-(S-*D*-Leu)-Phe-NHMe;

HS(*S*)$CH(PhtNBu)CH_2$-(S-*D*-Leu)-Phe-NHMe;

HS(*S*)$CH(PhtNEt)CH_2$-(S-*D*-Leu)-Phe-NHMe;

HS(1,2-Cyclopentyl)(S-*D*-Leu)-Phe-NHMe

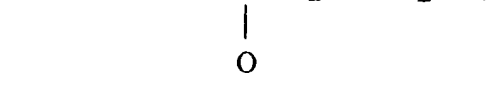
Me-S$(NH)_2$-(CH_2-DL-Leu)-Trp-NHBn;

n-Bu-S$(NH)_2$-(CH_2-DL-Leu)-Trp-NHBn;

n-Bu-S$(NH)_2$-(CH_2-DL-$TyrOCH_3$)-Trp-NHBn;

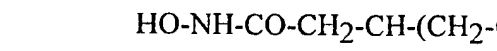
Me-RS-SO(NH)-(CH_2-L-Leu)-Phe-Ala-NH_2;

n-Bu-RS-SO(NH)-(CH_2-L-Leu)-Phe-Ala-NH_2;



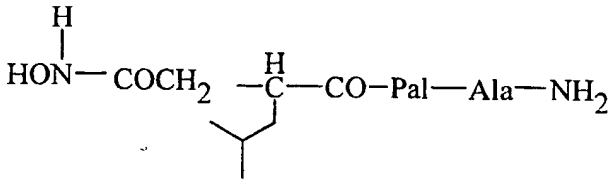
HONH-C-$CH_2CH(CH_2CH(CH_3)_2)$-CO-Nal-Ala-NH_2;

O

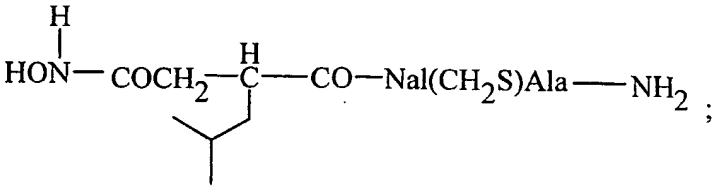


HO-NH-CO-CH_2-CH-(CH_2-$CH(CH_3)_2$-CO-Nal-Pro-NH_2;

HO-NH-CO-CH(CH_3-CH(CH_2)-CH(CH_3)$_2$)-CO-Nal-Ala-NH_2;

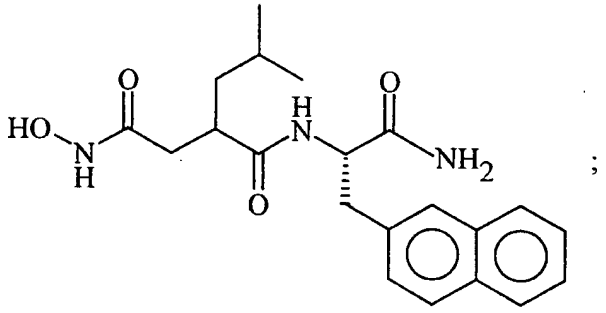


, wherein Pal is 3-pyridylalanine;



;

HO-NH-CO-CH_2-CH(CH_2CH(CH_3)$_2$)-CONal-(CH_2NH)-Ala-NH_2;



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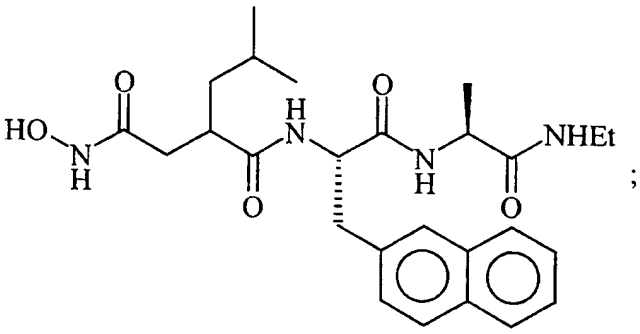

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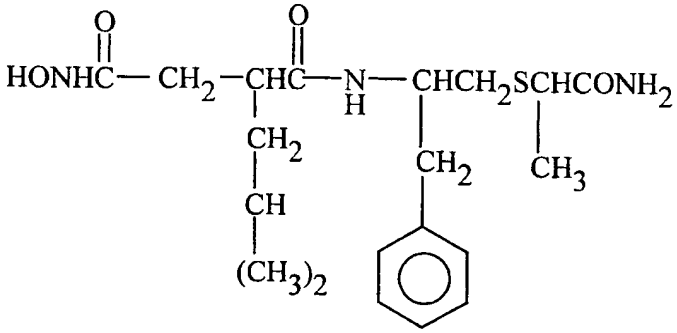

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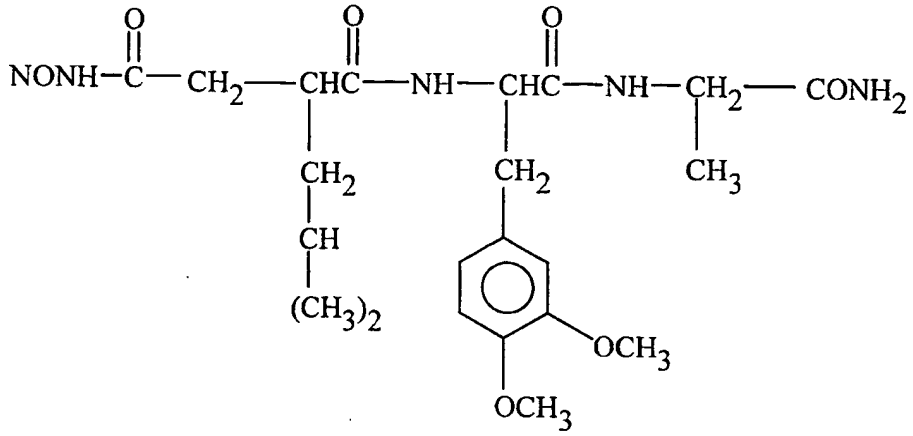


4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-morpholin-4-ylethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[methylamino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1H-imidazol-2-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1H-tetrazol-5-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[(2-(phenyl)ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(pyridin-3-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-methyl-2H-tetrazo-5-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-hydroxy-2-methyl-pyrimidin-5-ylmethyl)amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[2-(2-pyridin-3-yl)ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[1-(1H-tetrazol-5-yl)ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(5-amino-4H-[1,2,4]-triazol-3-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[1-(6-oxo-1,6-dihydro-pyridazin-3-yl)ethyl]amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(phenyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(pyridin-4-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[2-(1H-imidazol-4-yl)ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(pyridin-2-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-sulfamoyl-phenyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-sulfamoyl-phenyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-dimethylamino-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[1-(S)-phenyl-ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1,1-dioxo-tetrahydro-thiophen-3-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-sulfamoyl-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[1-(R)-phenyl-ethyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-fluorobenzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(furan-2-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1-methyl-1H-tetrazol-5-ylmethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1,2,3,4-tetrahydro-naphthalen-1-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2,4-difluoro-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-nitrobenzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-nitrobenzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-methanesulfonylamino-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-methanesulfonylamino-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3,4-difluoro-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-trifluoromethyl-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-[2-(S)-[1-(R)-Carboxy-3-(1,3-dioxo-1,3-dihydro-benzo[f]isoindol-2-yl)-propylamino]-4-methyl-pentanoylamino-methyl)-benzoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-hydroxy-1,1-bis-hydroxymethyl-ethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3,5-difluoro-benzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[benzylmethyl-amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-dimethylaminoethyl)-methyl-amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1-azabicyclo[2.2.2]-oct-3(R)-amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1-azabicyclo[2.2.2]oct-3-(S)-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-(R)-4-(S)-5-(R)-6-tetrahydrox-tetrahydra-pyran-2-(R)-ylmethyl)amino]-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(N,N′-dimethyl-hydrazino)carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(methylmethoxy)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(dimethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-oxo-tetrahydro-thiophen-3-(R)-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(2-oxo-tetrahydro-thiophen-3-(S)-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-(R)-acetylamino-4-(S)-5-(S)-dihydroxy-6-(R)-hydroxymethyl-tetrahydro-pyran-2-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[benzyl(2-hydroxyethyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[3,4-dihydro-1H-isoquinoline-2-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[4-methylpiperazine-1-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[1-oxo-[1,4]thiazinane-4-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[morpholine-4-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[4-(2-3-dihydroxy-propyl)-piperazine-1-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[3,4,5,6-tetrahydro-H-[2,3]bipyridinyl-1]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1-methyl-8-oxo-1,7-diazacyclotridec-9-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[methyl-1-methyl-piperidin-4-yl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(4-hydroxy-1,1-dioxo-tetrahydro-thiophen-3-yl)amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-(4-ethoxycarbonylmethyl-piperazine-1-carbonyl)butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(1,1-dioxo-tetrahydro-thiophen-3-yl)-methyl-amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[2-(R)-(pyridin-3-yl)-pyrrolidinecarbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[2-(S)-(pyridin-3-yl)-pyrrolidinecarbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[3-oxo-2-(R)-phenyl-piperazine-1-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[3-oxo-2-(S)-phenyl-piperazine-1-carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[(pyridine-3-carbonyl-hydrazino)carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(benzenesulfonyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(3-aminobenzyl)amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[4-(trifluoro-methanesulfonylamino)benzyl]amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[2-hydroxy-(R)-bicyclo[4.3.0]nona-3,6(1)-diene]amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[[2-hydroxy-(S)-bicyclo[4.3.0]nona-3,6(1)-diene]amino]carbonyl]butyl]-amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[[(N-methyl-pyrrolidine)-methyl-amino]carbonyl]butyl]amino]-butanoic acid;

4-(1,3-Dihydro-1,3-dioxo-2H-benz[f]isoindol-2-yl)-2-(R)-[[3-methyl-1-(S)-[(N-ethoxycarbonylmethyl-piperazine)-1-carbonyl]butyl]amino]-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-bromo-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-propoxy-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-nitro-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-amino-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-methyl-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-benzyloxy-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-phenyl-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-methanesulfonylamino-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-benzenesulfonylamino-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[1-(S)-(Benzylamino)carbonyl-3-methylbutylamino]-4-(5-hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-butanoic acid;

2-(R)-[[3-Methyl-1-(S)-[[(pyridin-3-ylmethyl)amino]carbonyl]-butyl]amino]-4-(1,3,5,7-tetraoxo-3,5,6-tetrahydro-1H-pyrolo[3,4-f]isoindol-2-yl)butanoic acid;

EtONHCONMe-CH_2CH(iBu)-CO-L-Trp-NHEt;

EtCONOH-CH_2CH(iBu)-CO-L-Trp-NHEt;

n-PrCONOEt-CH_2CH(iBu)-CO-L-Trp-NHEt;

EtNHCONOMe-CH_2CH(iBu)-CO-L-Trp-NHEt;

MeNHCONOH-CH_2CH(iBu)-CO-L-Trp-NHEt;

EtONHCONMe-CH_2CH(iBu)-CO-L-Ala(2-naphthyl)-NHEt;

EtCONOH-CH_2CH(iBu)-CO-L-Ala(2-naphthyl)-NHEt;

n-PrCONOEt-CH_2CH(iBu)-CO-L-Ala(2-naphthyl)-NHEt;

EtNHCONOMe-CH_2CH(iBu)-CO-L-Ala(2-naphthyl)-NHEt;

MeNHCONOH-CH_2CH(iBu)-CO-L-Ala(2-naphthyl)-NHEt;

HONHCONHCH$_2$CH(iBu)-CO-L-TrpNHMe;

HONHCONHCH$_2$CH$_2$CH(iBu)-CO-L-TrpNHMe;

HONHCONHCH(iBu)-CO-L-TrpNHMe;

H_2NCON(OH)CH(iBu)-CO-L-TrpNHMe;

N(OH)CH$_2$CH(iBu)-CO-L-TrpNHMe;

$H_2NCON(OH)CH_2CH_2CH(iBu)$-CO-L-TrpNHMe;

$CH_3CON(OH)CH(iBu)$-CO-L-TrpNHMe;

$CH_3CON(OH)CH_2CH(iBu)$-CO-L-TrpNHMe;

$CH_3CON(OH)CH_2CH_2CH(iBu)$-CO-L-TrpNHMe;

$NHOHCOCH_2CH(i\text{-}Bu)$CO-L-Trp-NHMe;

$HONHCONHCH_2CH(i\text{-}Bu)CONHCHCOOH$ or

$$\begin{array}{c} \\ | \\ R^4 \end{array}$$

$ROOCCH_2CH(i\text{-}Bu)CONHCHCOOH$;

$$\begin{array}{c} \\ | \\ R^4 \end{array}$$

N-{D,L-2-(Hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-(2′-naphthyl)alanyl-L-alanine, 2-(amino)ethyl amide;

N-{D,L-2-(Hydroxyaminocarbonyl)methyl-4-methylpentanoyl}-L-3-amino-2-dimethylbutanoyl-L-alanine, 2-(amino)ethyl amide;

4(S)-[3-Hydroxyaminocarbonyl-2(R)-(2-methylpropyl)propanoyl]amino-1,2,3,4,5-tetrahydro-3H-2-benzazepin-3-one;

[4-(N-Hydroxyamino)-(2R)-isobutyl-3-methylsuccinyl]-L-phenylglycine-N-methylamide;

4(S)-[2(R)-[1(R)-Hydroxycarbamoyl-2-morpholinoethyl]-4-methylvaleryl]amino-1,2,4,5-tetrahydro-3H-2-benzazepine-3-one;

(1R,4S)-4-[(2R)-Hydroxycarbamoylmethyl-4-methylvaleryl]amino-3-oxo-1,2,4,5-tetrahydro-3H-2-benzazepine-1-carboxylic acid;

3-[2-(N-Methylcarbamoyl)ethylsulfinyl]-5-methylhexanohydroxamic acid;

N-[(2-Thenoylmercapto-3-methyl)-butanoyl]-homocysteine thiolactone;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-isoleucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-alanine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-phenylalanine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-serine-O-benzyl ether, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-tryptophan, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(2-phenyl-ethyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-norleucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-valine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-serine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-asparagine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-threonine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-lysine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-glutamic acid, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-tyrosine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-5-(1,3-dioxo-isoindolin-2-yl)pentyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-5-(1-oxo-isoindolin-2-yl)pentyl]-α-(S)-(2-phenyl-ethyl)-glycine-(S)-leucine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-5-(1-oxo-isoindolin-2-yl)pentyl]-α-(S)-(2-phenyl-ethyl)-glycine-(S)-arginine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(3-hydroxyphenyl)-ethyl)glycine-(S)-leucine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(4-methylphenyl)-ethyl)glycine-(S)-leucine, N-phenylamide hydrochloride;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(2′-thienyl)ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(4-ethylphenyl)ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-5-(1-oxo-isoindolin-2-yl)pentyl]-α-(S)-(2-(4-propylphenyl)ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(4-chlorophenyl)ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(2-cyclohexyl-ethyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(cyclohexyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(cyclohexylmethyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-β-naphthylalanine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-α-naphthylalanine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-[(L)-glutamic acid, α,δ-bis-N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-cyclohexylamide;

N-[(1(R)-Carboxy-ethyl)]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(4-hydroxyphenyl-ethyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-phenylglycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-glutamic acid, N_{δ}-benzylamide, N_{α}-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-ornithine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-arginine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-(3-phenylpropyl)glycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-α-(S)-n-octylglycine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-(4-carboxyphenyl)amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-(4-trifluoromethylphenyl)amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-(3-pyridyl)amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-phenyl-ethyl)glycine-(L)-leucine, N-(benzothiazol-2-yl)amide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(4-n-propylphenyl)ethyl)glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-4-propylphenyl)ethyl)glycine-(L)-arginine, N-phenylamide;

N-[1(R)-Carboxy-ethyl]-α-(S)-(2-(3,4-dimethylphenyl-ethyl)glycine-(L)-leucine, N-phenylamide;

(2-(((4-(1,3-Dihydro-1,3-dioxo-2H-isoindol-2-yl)butyl)-hydroxyphosphinyl)methyl)-4-phenylbutanoyl)-L-leucine, N-phenylamide;

(2-(((4-(1,3-Dihydro-1-oxo-2H-isoindol-2-yl)butyl)-hydroxyphosphinyl)methyl)-4-phenylbutanoyl)-L-leucine, N-phenylamide;

(2-(((4-(1,3-Dihydro-1-oxo-2H-isoindol-2-yl)butyl)(2-methyl-1-(1-oxopropoxy)propoxy)phosphinyl)methyl)-4-phenylbutanoyl)-L-leucine, N-phenylamide;

(2-((Hydroxy(methyl)phosphinyl)methyl)-4-phenylbutanoyl)-L-leucine, N-phenylamide;

[[Hydroxy[1(R)-[N-(N-acetyl-L-prolyl-L-alanyl)-amino]-ethyl]-phosphinyl]-methyl]-4-phenyl-butanoyl-L-leucyl, N-phenylamide;

[Hydroxy-[N-(N-(benzoyl)-L-prolyl)aminobutyl]phosphinyl]methyl]-4-phenyl-butanoyl-L-leucine, N-phenylamide;

[Hydroxy-[2-Methylpropyloxycarbonyl-aminobutyl]-phosphinyl]methyl]-4-phenylbutanoyl-L-leucine, N-phenylamide;

[Hydroxy-[1-Methylethylaminocarbonyl-aminobutyl]-phosphinyl]methyl]-4-phenylbutanoyl-L-leucine, N-phenylamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-leucinamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-leucine, N-phenylamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-leucine, N-benzylamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-leucine, N-(2-phenylethyl)amide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-phenylalaninamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-phenylalanine N-phenylamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-phenylalanine N-benzylamide;

N-(2-Thiomethyl-4-phenylbutanoyl)-(L)-phenylalanine-b-alanine;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(2(S)-t-butyl)glycine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(2(S)-t-butyl)glycine, N-(4-pyridylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(L-arginine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(2(S)-t-butyl)glycine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(2(S)-(4-thiazolylmethyl)glycine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(2(S)-(3-pyridylmethyl)glycine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-(4-pyridyl)amide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(2(S)-(2-pyridylmethyl)glycine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-arginine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-phenylalanine, N-4-pyridylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(1-(4-(N-(2-oxoisoindolinyl))-butyl))-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(1-(4-(N-(2-oxoisoindolinyl))-but-2-enyl))-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(4-Fluorophenyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(Phenyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(4-Methoxyphenyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, phenylamide)amide;

2(R)-(2-(4-(4-Methylphenyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, phenylamide)amide;

2(R)-(2-(4-(4-Hydroxy-n-butyl)-phenyl)-ethyl)-4-methylpentanedioic acid 1-(S-leucine, phenylamide)amide;

2(R),4(S)-(2-(4-(3-Hydroxy-n-propyl)phenyl)ethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-Phenylethyl)-4-methyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(L-leucine, N-ethylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-(L-leucine, N-isopropylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)propyl)-1,5-pentanedioic acid 1-(2(S)-tert-butyl-glycine, N-4-pyridyl)amide)amide;

2(R)-(3-(4-(1-n-Propyl)phenyl)propyl)-1,3-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-hexyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-butyl-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(3-methylbenzyl)-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-(2-benzimidazolyl)butyl)-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-(2-benzthiazolyl)butyl)-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-(2-benzoxazolyl)butyl)-1,5-pentanedioic acid 1-(L-leucine, N-phenylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-phenylamide)amide 9-piperidineamide;

2(R)-(2-(4-(1-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-phenylamide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-tert-butylamide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-benzylamide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-morpholineamide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-(1(R)-phenylethyl)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-(1(S)-phenylethyl)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-(N-methyl-N-phenyl)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-(N'-methylpiperazine)amide trifluoroacetic acid salt;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide 9-(3-pyridyl)amide;

2(R)-(2-(4-(1-Propyl)phenyl)ethyl)-4-carboxy-1,9-nonanedioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-((R)-(S-p-methoxybenzyl)penicillamine, N-phenylamide)amide;

2(R)-(2-(4-(1-Propyl)phenyl)ethyl)-1,5-pentanedioic acid 1-((R)-(S-p-methoxybenzyl)penicillamine sulfone, N-phenylamide)amide;

2-(2-(4-(1-Propyl)phenyl)ethyl)-4-(1-(4-(2-phthalimido))butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-benzoylamino-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-pivaloylamino-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-phenylsulfonylamino-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-(N'-phenylureido)-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-phenyloxycarbonylamino-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-N'-benzyloxycarbonylamino-L-prolylamino)-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-cyclopentylamino-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-(2-carboxybenzoylamino)-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-methylamide)amide;

2(R)-(2-(4-(1-n-Propyl)phenyl)ethyl)-4-(4-cyano-1-butyl)-1,5-pentandioic acid 1-(L-leucine, N-phenylamide)amide;

N-[1(R)-Carboxyethyl]-α-(S)-(9-amino-n-nonyl)]glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxyethyl]-α-(S)-(n-octyl)]glycine-(L)-leucine, N-phenylamide;

N-[1(R)-Carboxyethyl]-α-(S)-(n-octyl)]glycine-(L)-arginine, N-phenylamide;

N-[1(R)-Carboxyethyl]-α-(S)-(9-amino-n-nonyl)]glycine-(L)-arginine, N-phenylamide;

N-[1(R)-Carboxyethyl]-α-(S)-(n-decyl)]glycine-(L)-leucine, N-phenylamide;

1-(2-(4-Propylphenyl)ethyl)cyclopentane-1,3-dicarboxylic acid 1-(L-leucine, N-phenylamide)amide;

1-(2-(4-Propylphenyl)ethyl)cyclohexane-1,3-dicarboxylic acid 1-(L-leucine, N-phenylamide)amide;

N-[1(R)-Carboxyethyl]-α-(S)-2-(4-fluorobiphenyl)-glycyl-(S)-2-(*tert*-butyl)glycine, N-phenylamide;

3S-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxy-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutyl-3S-acetylthiomethylsuccinyl]-amino-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]amino-1-methoxy-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxymethyl-3,4-dihydrocarbostyril;

1-Carboxymethyl-3S-[4-N-hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]amino-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxyethoxymethyl-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-heptylsuccinyl]amino-1-methoxy-3,4-dihydrocarbostyril;

7-Chloro-3S-[4-(N-hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxymethyl-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxyethyl-3,4-dihydrocarbostyril;

3S-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxyethyl-6,7-methylenedioxy-3,4-dihydrocarbostyril;

3R-[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]amino-1-methoxyethyl-6,7-methylenedioxy-3,4-dihydrocarbostyril;

2-(R)-N-Hydroxy-2-[(4-methoxybenzenesulfonyl) (3-morpholin-4-yl-3-oxopropyl)amino]-3-methyl-butyramide;

2-(R)-2-[(2-Benzylcarbamoylethyl)(4-methoxy-benzenesulfonyl)-amino]-N-hydroxy-3-methylbutyramide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl) (2-[(pyridin-3-ylmethyl)carbamoyl]ethyl)amino)-3-methylbutyramide;

2-(R)-N-Hydroxy-2-([4-methoxybenzenesulfonyl]-[2-(methylpyridin-3-ylmethylcarbamoyl)ethyl]amino)-3-methylbutyramide;

4-(3-[1-(R)-1-Hydroxycarbamoyl-2-methylpropyl)-(4-methoxybenzenesulfonyl)amino]propionyl)piperazine-1-carboxylic acid, tert-butyl ester;

2-(R)-N-Hydroxy-2-[(4-methoxybenzenesulfonyl)(3-oxo-3-piperazin-1-ylpropyl)amino)-3-methylbutyramide hydrochloride;

2-(R)-2-[(Benzylcarbamoylethyl)(4-methoxy-benzenesulfonyl)amino]-N-hydroxy-3-methylbutyramide;

2-(R)-N-Hydroxy-2-[(4-methoxybenzenesulfonyl][(2-morpholin-4-ylethylcarbamoyl)methyl]amino]-3-methylbutyramide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl) ([(pyridin-3-ylmethyl)-carbamoyl]methyl)amino)-3-methylbutyramide;

2-(R)-3,3,3,-Trifluoro-N-hydroxy-2-[(methoxy-benzenesulfonyl)(3-morpholin-4-yl-3-oxopropyl)amino]propionamide;

2-(R)-N-Hydroxy-2-((4-phenoxybenzenesulfonyl)[2-methylpyridin-4-ylmethylcarbamoyl)ether]amino)-3-methylbutyramide;

4-[4-Methoxybenzenesulfonyl)(3-morpholin-4-yl-3-oxopropyl)amino]-1-methylpiperidene-4-carboxylic acid hydroxyamide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl)-[3-(4-methylpiperazin-1-yl)-3- oxopropyl]amino)-3-methylbutyramide;

2-(R)-2-[(2-Carboxyethyl)(4-methoxybenzene-sulfonyl)amino]-N-hydroxy-3-methylbutyramide;

[(2-Carboxyethyl)(3,4-dimethoxybenzene-sulfonyl)amino]-N-hydroxy-acetamide;

2-(R)-2-[(2-Carbamoylethyl)(4-methoxybenzene-sulfonyl)amino]-N-hydroxy-3-methylbutyramide;

2-(R), 3-(R)-3, N-Dihydroxy-2-[(4-methoxybenzenesulfonyl)(3-oxo-3-piperidin-1-ylpropyl)amino]-butyramide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl)[3-(methylpyridin-3-ylmethylcarbamoyl)propyl]amino)-3-methylbutyramide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl)[2-(methylcarboxymethylcarbamoyl)ethyl]amino)-3-methyl-butyramide;

2-(R)-N-Hydroxy-2-((4-methoxybenzenesulfonyl)[(1-methylpiperidin-4-ylcarbamoyl)methyl]amino)-3-methylbutyramide;

2-(R)-N-Cyclohexyl-N-hydroxy-2-((4-methoxy-benzenesulfonyl)-[3-(4-methylpiperazin-1-yl)-3-oxopropyl]amino)-acetamide;

2-(R)-N-Hydroxy-2-[(methoxybenzenesulfonyl)(3-morpholin-4-yl-[3-oxopropyl)amino]-4-(morpholin-4-yl)butyramide;

[4-N-Benzyloxyamino)-2(R)-isobutylsuccinyl]-L-leucyl-L-alanine ethyl ester;

[4-N-Benzyloxyamino)-2(R)-isobutylsuccinyl]-3(RS)-aminolaurolactam;

N^a-[4-(N-Benzyloxyamino)-2(R)-isobutylsuccinyl]-N^e-(N-benzyloxycarbonylglycyl)-L-lysyl-L-alanine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylglycine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylglycine isopentylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-valylglycine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylglycine ethylamide;

N^a-[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-N^e-tert.butoxycarbonyl-L-lysylglycine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-O-methyl-L-tyrosinylglycine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-O-methyl-L-tyrosinylglycine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucyl-L-alanine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylglycine isopentyl ester;

[4-(N-Hydroxyamino)-2(R)-propylsuccinyl]-L-leucylglycine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-sec.butylsuccinyl]-L-leucylglycine ethyl ester;

[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-L-leucyl-L-alanine;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylglycine methyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucylsarconsine ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucyl-L-proline ethyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucine-L-alanine isopropyl ester;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucine-2-oxopropylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucine-2-methoxyethylamide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-leucine-2,2-dimethoxyethylamide;

N^a-[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-N^e-glycyl-L-lysine methylamide;

N^a-[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-N^e-(4-carboxybenzoyl)-L-lysl-L-alanine ethyl ester;

N^a-[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-N^e-(4-carboxybenzoyl)-L-lysyl-L-aline;

[4-(N-Hydroxyamino)-2(R)-isobutylsuccinyl]-3(RS)-aminooctahydro-2H-azonin-2-one;

[4-(N-Hydroxyamino)-3(S)-methyl-2(R)-isobutyl-succinyl]-L-leucylglycine ethyl ester;

[(3-Aminophthalimido)methyl][(RS)-4-methyl-2-[[(S)3-methyl-1-(methylcarbamoyl)butyl]carbamoyl]pentyl]phosphinic acid;

[(RS)-4-Methyl-2-[[(S)-3-methyl-1-(methyl-carbamoyl)butyl]-carbamoyl]pentyl](1,8-naphthalenedi-carboximidomethyl)phosphinic acid;

[(R or S)-4-Methyl-2-[[(R or S)-2-oxo-3-azacyclotridecyl]-carbamoyl]pentyl](1.8-naphthalenedicarboximidomethyl)phosphinic acid;

N-[N-[(R or S)-2[[[[[N-[1-(Benzyloxy)carbonyl]-L-prolyl]-L-leucyl]amino]methyl]hydroxyphosphinyl]-methyl]-4-methylvaleryl]-L-leucyl]-L-alanine;

[[1,4-Dihydro-2,4-dioxo-3(2H)-quinazolinyl]-methyl][[(R or S)-4-methyl-2-[[(R or S)-2-oxo-3-azacyclotridecyl]carbamoyl]pentyl]phosphinic acid;

N^2-[(R)-Hydroxycarbamoylmethyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

N^2-[2(R or S)-[[[(5-Bromo-2,3-dihydro-6-hydroxy)-1,3-dioxo-1H-benz[d,e]isoquinol-2-yl)methyl]-[(hydroxy)phosphinyl]methyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

N^2-[(R or S)-[[(R)-(Amino)[(5-bromo-2,3-dihydro-6-hydroxy-1,3-dioxo-1H-benz[d,e]isoquinol-2-yl)methyl](hydroxy)phosphinyl]methyl]-4-methylvaleryl]-N^3,1-dimethyl-L-valinamide hydrobromide;

N^2-[2(R or S)-[1(S)-(Hydroxycarbamoyl)ethyl-4-methylvaleryl]-N^1,3-dimethylvalinamide;

N^2-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-phthalimidoethyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

N^2-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-4-(methoxy-carbonyl)butyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

M^2-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-4-phenyl-butyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

N^2-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-succinimidoethyl]-4-methylvaleryl]-N^1,3-dimethyl-L-valinamide;

4-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-phthalimidoethyl]-4-methylvaleryl]morpholine;

4-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-phthalimidoethyl]-4-methylvaleryl]tetrahydro-1,4-thiazine;

1-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-phthalimidoethyl]-4-methylvaleryl]-4-piperidinol;

1-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-(1,2-dimethyl-3,5-dioxo-1,2,4-triazolidin-4-yl)ethyl]-4-methylvaleryl]piperidine;

4-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-2-(3-methyl-2,5-dioxo-1-imidazolidinyl)ethyl]-4-methylvaleryl]tetrahydro-1,4-thiazine;

Hexahydro-2-[2(R)-[1(R or S)-(hydroxycarbamoyl)-2-phthalimidoethyl]-4-methylvaleryl]-N-methyl-3(S)-pyridazinecarboxamide;

1-[2(R)-(R or S)-(Hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]-4-methylvaleryl]-4-piperidinol;

[4-(N-Hydroxyamino)-2(R or S)-heptylsuccinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(R or S)-nonylsuccinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(R or S)-heptyl-3(S)-methylsuccinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(R)-heptyl-3(R or S)-(phthalimidomethyl)-succinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-nonylsuccinyl]-L-tert.butylglycine methylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-phenylalanine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptyl-3(R or S)-phthalimidomethyl)-succinyl]-L-tert.butylglycine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptyl-3(R or S)-(3-phenylpropyl)-succinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-leucine methylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-leucine neopentylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-alanyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-(N^e-phthaloyl)-lysyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-undecylsuccinyl]-L-leucyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-phenylalanyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-nonalyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-phenylalanine tert.butylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-tert.butylglycine methylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-neopentylglycine methylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-homophenylalanyl-L-leucine ethylamide;

[4-(N-Hydroxyamino)-2(RS)-heptylsuccinyl]-L-cyclohexylalanine methylamide;

[4-(N-Hydroxyamino)-2(RS)-isooctylsuccinyl]-L-phenylalanine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptylsuccinyl]-L-neonpentylglycine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptylsuccinyl]-(D or L)-β,β-dimethylphenylalanine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptylsuccinyl]-(D or L)-threo-β-methylphenylalanine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptylsuccinyl]-DL-erthro-β-methylphenylalanine methylamide;

[4-(N-Hydroxyamino)-2(R)-heptyl-3(R or S)-[(3-methyl-2,5-dioxo-1-imidazolidinyl)methyl]succinyl]-L-leucyl-L-leucine ethylamide;

N^2-[3-Cyclobutyl-2(R or S)-[(hydroxycarbamoyl)-methyl]-propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclopropyl-2(R or S)-[(hydroxycarbamoyl)-methyl]-propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclopentyl-2(R or S)-[(hydroxycarbamoyl)-methyl]-propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclopropyl-2(R)-[1(R or S)-[(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclopropyl-2(R)-[1(R or S)-[(hydroxy-carbamoyl)-4-phenylbutyl)]propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-4-phenylbutyl]propionyl]-N^1,3-dimethyl-L-valinamide;

N^2-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-4-phenylbutyl]propionyl]-N^1,3-dimethyl-L-valinamide;

1-[3-Cyclopropyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]piperidine;

1-[3-Cyclopropyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-4-piperidinol;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]piperidine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-4-piperidinol;

1-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-4-piperidinol;

1-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]piperidine;

3-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-3-azabicyclo[3.2.2]nonane;

3-[3-Cyclopropyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-3-azabicyclo[3.2.2]nonane;

3-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-3-azabicyclo[3.2.2]nonane;

1-[3-Cyclohexyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]piperidine;

4-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]tetrahydro-1,4-thiazine;

4-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]tetrahydro-1,4-thiazine S,S-dioxide;

4-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]tetrahydro-1,4-thiazine;

3-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-5,5-dimethyl-N-propyl-[4(R)-thiazolidinecarboxamide;

4-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]morpholine;

3-[3-Cyclopentyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-N,5,5-trimethyl-4(R)-thiazolidinecarboxamide;

4-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-4-phenylpiperazine;

4-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]morpholine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxy-carbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]pyrrolidine;

8-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-1,4-dioxa-8-azaspiro[4,5]decane;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]-4-methoxypiperidine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]octahydroazocine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(5,5-dimethyl-2,4-dioxo-3-oxazolidinyl)ethyl]propionyl]piperidine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]propionyl]hexahydroazepine;

1-[3-Cyclobutyl-2(R)-[2-(hexahydro-1,3-dioxo-pyrazolo[1,2-a][1,2,4]-triazol-2-yl)-1(R or S)-(hydroxycarbamoyl)ethyl]propionyl]piperidine;

1-[3-Cyclobutyl-2(R)-[1(R or S)-(hydroxycarbamoyl)-2-phthalimidoethyl]propionyl]piperidine;

2-[2(R)-[1(R or S)-(Hydroxycarbamoyl)-4-phenylbutyl]nonanoyl]-hexahydro-N-methyl-3(S)-pyridazinecarboxamide;

N-Cyclohexyl-hexahydro-2-[2(R)-[1(RS)-(hydroxycarbamoyl)-4-phenylbutyl]nonanoyl]-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R)-[1(RS)-(hydroxycarbamoyl)-4-phenylbutyl]nonanoyl]-N-(2,2,6,6-tetramethyl-4-piperidinyl)-3(S)-pyridazinecarboxamide;

1-[2(R)-[1(R or S)-Hydroxycarbamoyl)-4-phenylbutyl]nonanoyl]-piperidine;

N^2-[2(R)-[1(RS)-(Hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]nonanoyl]-N^1-methyl-L-prolinamide;

1-[2(R)-[l(R or S)-(Hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]nonanoyl]piperidine;

Hexahydro-2-[2(R)-1(R or S)-(hydroxycarbamoyl)-2-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)ethyl]nonanoyl]-N-methyl-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[1(S)-(hydroxycarbamoyl)-3-phenylpropyl]-undecanoyl]-N-methyl-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[1(S)-(hydroxycarbamoyl)-3-phenylpropyl]-undecanoyl]-N-methoxy-N-methyl-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[(1(S)-(hydroxycarbamoyl)-3-phenylpropyl]-undecanoyl]-N-(1,2,2,6,6-pentamethyl-4-piperidinyl)-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[1(S)-(hydroxycarbamoyl)ethyl]undecanoyl]-N-methyl-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[1(S)-(hydroxycarbamoyl)-3-phenylpropyl]-nonanoyl]-N-methyl-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[1(S)-(hydroxycarbamoyl)ethyl]nonanoyl]-N-methyl-3(S)-pyridazinecarboxamide;

1-[2(R or S)-[l(S)-(Hydroxycarbamoyl)ethyl]undecanoyl]piperidine;

1-[2-(R or S)-[1(S)-(Hydroxycarbamoyl)-3-phenylpropyl]undecanoyl]-piperidine;

Hexahydro-2-[2(R or S)-[l(S)-(hydroxycarbamoyl)-3-phenylpropyl]-undecanoyl]-N-(2,2,6,6-tetramethyl-4-piperidinyl)-3(S)-pyridazinecarboxamide;

Hexahydro-2-[2(R or S)-[l(S)-(hydroxycarbamoyl)ethyl]undecanoyl]-N-(2,2,6,6-tetramethyl-4-piperidinyl)-3(S)-pyridazinecarboxamide;

1-[2(R or S)-[1(S)-(hydroxycarbamoyl)-4-phenylbutyl]undecanoyl]-piperidine;

4-[2(R or S)-[1(S)-(hydroxycarbamoyl)-4-phenylbutyl]undecanoyl]-morpholine;

1-(Benzyloxycarbonyl)-hexahydro-2-[2(R)-[(R or S)-(hydroxycarbamoyl)-4-phenylbutyl]nonanoyl]-N-(α(S)-methylbenzyl)-3(S)-pyridazinecarboxamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-5-(carboxy)pentanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(propylamino)-6-(oxo)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-(6RS)-6-(hydroxy)heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2-[(2'R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(hydroxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2-[(2'R)-2′-[2′-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2′R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(4′-oxobutylamino)hexanoyl]-L-phenylalanine N-methylamide;

2(S)-N-2-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[(1′S)-1′-(Methyl)-2′-(hydroxyamino)-2′-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[(1′S)-1′-(Methyl)-2′-(hydroxyamino)-2′-(oxo)ethyl]-6-(oxo)-6-(propylamino)hexanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2[(2′R)-[(1″R)-1″-(1,3-Dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl-2″-(hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]-amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(oxo)-6-(propylamino)hexanoyl]-L-phenylalanine N-2-phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hyroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3-cyclohexylpropionic acid N-2-(4′-sulfamoyl)phenylethylamide;

N-[2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6′-(phenylmethoxy)-hexanoyl]-L-(3,5-dimethyl)phenylalanine N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methoxy)phenoxy]hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methyl)phenoxy]hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(1-oxo)butylamino]hexanoyl]amino-3-cyclohexylpropionic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(2-Methylpropyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenoxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-(phenoxy)heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-5-(phenylmethoxy)-pentanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-(phenylmethoxy)-heptanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenyloxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-[(phenyloxy)heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(2-phenethylamino)-6′-(oxo)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methylphenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-chlorophenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(3-methylphenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-(carboxymethyl)-6′-(3-methylphenoxy)hexanoyl]-amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-5-(carboxy)pentanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenylmethoxy)-hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(propylamino)-6-(oxo)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-(6RS)-6-(hydroxy)-heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(hydroxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2′R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(4′-oxobutylamino)hexanoyl]-L-phenylalanine N-methylamide;

2(S)-N-2-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[(1′S)-1′-(Methyl)-2′-(hydroxyamino)-2′-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[(1′S)-1′-(Methyl)-2′-(hydroxyamino)-2′-(oxo)ethyl]-6-(oxo)-6-(propylamino)hexanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2[(2′R)-[(1″R)-1″-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl-2″-(hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]-amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(oxo)-6-(propylamino)hexanoyl]-L-phenylalanine N-2-phenylethylamide;

(2S)-N-2-[(2'R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6′-(oxo)-6′-(propylamino)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3-cyclohexylpropionic acid N-2-(4′-sulfamoyl)phenylethylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6′-(phenylmethoxy)-hexanoyl]-L-(3,5-dimethyl)phenylalanine N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methoxy)phenoxy]hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methyl)phenoxy]hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(1-oxo)butylamino]hexanoyl]amino-3-cyclohexylpropionic acid N-2-(4′-sulfamoyl)phenylethylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(Methyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2-[(2′R)-2′-[(1″S)-1″-(2-Methylpropyl)-2″-(hydroxyamino)-2″-(oxo)ethyl]-6-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenoxy)hexanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-(phenoxy)heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-phenylethylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-(phenylmethoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-2-(4′-sulfamoyl)phenylethylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-5-(phenylmethoxy)pentanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-(phenylmethoxy)heptanoyl]-L-phenylalanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-6-(phenyloxy)hexanoyl]-L-phenylelanine N-methylamide;

N-[(2R)-2-[2′-(Hydroxyamino)-2′-(oxo)ethyl]-7-[(phenyloxy)heptanoyl]-L-phenylalanine N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(2-phenethylamino)-6′-(oxo)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-methylphenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(4-chlorophenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-[2″-(Hydroxyamino)-2″-(oxo)ethyl]-6′-[(3-methylphenoxy)hexanoyl]amino-3,3-dimethylbutanoic acid N-methylamide;

(2S)-N-2′-[(2′R)-2′-(Carboxymethyl)-6′-(3-methylphenoxy)hexanoyl]-amino-3,3-dimethylbutanoic acid N-methylamide;

(3*R*,10*S*)-5-Methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanoic acid;

(3*R*,10*S*)-*N*-Hydroxy-5-methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]-nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanamide;

(3*R*,11*S*)-*N*-Hydroxy-5-methyl-3-(10-oxo-1,9-diazatricyclo[11.6.1.0]-eicosa-13(20),14(19),15,17-tetraen-11-ylcarbamoyl)hexanamide;

(3*R*,9*S*)-5-Methyl-3-(8-oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12(17),13,15-tetraen-9-ylcarbamoyl)hexanoic acid;

(3*R*,9*S*)-*N*-Hydroxy-5-methyl-3-(8-oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12(17),13,15-tetraen-9-ylcarbamoyl)hexanamide;

(10*S*)-[4-Methyl-2-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)pentyl]-(quinolin-2-ylthiomethyl)phosphinic acid;

(3*R*,10*S*)-*N*-Hydroxy-5-methyl-2-methoxycarbonyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)-hexanamide;

N-(4-Methyl-2-carboxymethylpentanoyl)-L-leucine-*N*′-(4-methoxycarbonylphenyl)carboxamide;

N-(4-Methyl-2-(*N*″-hydroxycarbamoyl)methylpentanoyl)-L-leucine-*N*′-(4-methoxycarbonylphenyl)carboxamide;

N-(4-Methyl-2-(*N*″-hydroxycarbamoyl)methylpentanoyl)-L-leucine-*N*′-(4-carboxyphenyl)carboxamide;

N-(4-Methyl-2-(*N*″-hydroxycarbamoyl)methylpentanoyl)-L-tryptophan-*N*′-(4-carboxyphenyl)carboxamide;

N-(4-Methyl-2-(*N*″-hydroxycarbamoyl)methylpentanoyl)-L-cyclohexylglycine-*N*′-(4-methoxycarbonylphenyl)carboxamide;

N-(4-Methyl-2-(*N*″-hydroxycarbamoyl)methylpentanoyl)-L-*t*-leucine-*N*′-(4-methoxycarbonylphenyl)carboxamide;

(3*R*,10*S*)-6-Biphenyl-4-yl)-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]onadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanoic acid;

(3*R*,10*S*)-3-(9-Oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)-5-(thiophen-2-yl)pentanoic acid;

(3*R*,10*S*)-3-Cyclopentyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)propionic acid;

(3*R*,10*S*)-4-Cyclopentyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)butanoic acid;

(3*R*,10*S*)-4-Cyclopropyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)butanoic acid;

(3*R*,10*S*)-5-Methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanoic acid;

(3*R*,10*S*)-*N*-Hydroxy-5-methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]-nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanamide;

(3*R*,11*S*)-*N*-Hydroxy-5-methyl-3-(10-oxo-1,9-diazatricyclo[11.6.1.0]-eicosa-13(20),14(19),15,17-tetraen-11-ylcarbamoyl)hexanamide;

(3*R*,9S)-*N*-5-Methyl-3-(8-oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12(17),13,15-tetraen-9-ylcarbamoyl)hexanoic acid;

(3*R*,9*S*)-*N*-Hydroxy-5-methyl-3-(8-oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12(17),13,15-tetraen-9-ylcarbamoyl)hexanamide;

(10*S*)-2-Mercaptomethyl-4-methyl-*N*-(9-oxo-1,8-diazatricyclo[10.6.1.0]-nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)pentanamide;

(10*S*)-2-Acetylthiomethyl-4-methyl-*N*-(9-oxo-1,8-diazatricyclo[10.6.1.0]-nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)pentanamide;

(3*R*,10*S*)-2-(Methanesulfonamidomethyl)-5-methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)-hexanoic acid;

(3*R*,10*S*)-2-(3-Ethylureidomethyl)-5-methyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)hexanoic acid;

(3*R*,9*S*)-N-Hydroxy-2-hydroxy-5-methyl-3-(8-oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12(17),14,16-tetraen-9-ylcarbamoyl)hexanamide or its (2S,3R,9S) stereoisomer;

(3*R*,10*S*)-*N*-Hydroxy-5-methyl-2-methoxycarbonyl-3-(9-oxo-1,8-diazatricyclo[10.6.1.0]nonadeca-12(19),13(18),14,16-tetraen-10-ylcarbamoyl)-hexanamide;

(3R,9S)-5-Methyl-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-Cyclobutylmethyl-N-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)succinamic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-5-phenoxy-pentanoic acid;

(3R,9S)-5-(4-Chlorophenoxy)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)pentanoic acid;

(3R,9S)-5-(4-Chlorophenoxy)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)pentanoic acid ethyl ester;

(3R,9S)-3-(8-Oxo-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)pentanoic acid ethyl ester;

(3R,9S)-6-(4-Hydroxy-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-pyridin-4-yl-hexanoic acid;

(3R,9S)-6-[4-(3-Hydroxy-propoxy)-phenyl]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-5-(4-phenoxy-phenyl)pentanoic acid;

(3R,9S)-6-[4-(2-Hydroxy-ethoxy)-phenyl]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-[4-(2-pyrrolidin-1-yl-ethoxyphenyl]hexanoic acid;

(3R,9S)-6-(4-Methoxy-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-[4-(2-Methoxy-ethoxy)-phenyl]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-5-phenyl-pentanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-phenyl-hexanoic acid;

(3R,9S)-6-(3-Hydroxy-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-[4-(3-piperidin-1-yl-propoxy)phenyl]hexanoic acid;

(3R,9S)-6-[4-(3-Dimethylamino-propoxy)-phenyl]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-[4-(2-Dimethylamino-ethoxy)-phenyl]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-(4-Cyano-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-Naphthalen-2-yl-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-(4-pyrrol-1-yl)hexanoic acid;

(3R,9S)-6-(4-Hydroxy-3-methyl-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-(4-Benzyloxy-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-6-[4-(4-Aminobutoxy-phenyl)]-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-5-(4-Methoxy-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)pentanoic acid;

(3R,9S)-6-(4-Amino-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]-octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

(3R,9S)-3-(8-Oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)-6-[4-(pyridin-4-ylmethoxy)phenyl]-hexanoic acid;

(3R,9S)-6-(4-Acetylamino-phenyl)-3-(8-oxo-4-oxa-1,7-diazatricyclo[9.6.1.0]octadeca-11(18),12,14,16-tetraen-9-ylcarbamoyl)hexanoic acid;

N^{α}-[[3-(N-Hydroxycarbamoyl)-4-methylthio-2-propoxymethyl]butylyl]-N,O-dimethyltyrosine amide;

N^{α}-[[3-(N-Hydroxycarbamoyl)-4-isopropylthio-2-propoxymethyl]-butylyl]-N,O-dimethyltyrosine amide;

N^{α}-[[3-(N-Hydroxycarbamoyl)-2-propylthio]butylyl]-N,O-dimethyltyrosine amide;

N-[N-(1-Phosphono-3-phenylpropyl)-(S)-leucyl]-(S)-phenylalanine-N-methylamide;

N-[N-(1-Phosphono-3-(4-bromo-1,8-naphthalene-dicarboximido)propyl)-(S)-leucyl]-(S)-phenylalanine methylamide;

N-[N-(1-Phosphono-3-(benzyloxycarbonylamino)propyl)-(S)-leucyl]-(S)-phenylalanine methylamide;

N-[N-(1-Phosphono-3-(2-hydroxyphenyl)propyl)-(S)-leucyl]-(S)-phenylalanine methylamide;

N-[N-(1-Phosphono-3-(methylmercapto)propyl)-(S)-leucyl]-(S)-phenylalanine-N-methylamide;

N-[N-(1-Phosphono-3-(methylsulphinyl)propyl)-(S)-leucyl]-(S)-phenylalanine-N-methylamide;

N-[N-(1-Phosphono-3-(methylsulphonyl)propyl)-(S)-leucyl]-(S)-phenylalanine-N-methylamide;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(S)-tryptophan-N-methylamide;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(S)-lysine-N-methylamide;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(-)-aminoazacyclotridecan-2-one;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(S)-lysine-N-(aminoethyl)amide;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(S)-lysine-N-(ethylpyrrolidine)amide;

N-[N-(1-Phosphono-3-(1,8-naphthalenedicarboximido)propyl)-(S)-leucyl]-(S)-lysine-N-(ethyl-N-methylpiperazine)amide;

N-[N-(1-Phosphono-3-[8-(7,9-dioxo-8-azaspiro[4,5]decyl)]propyl)-(S)-leucyl]-(S)-phenylalanine-N-methylamide; and

N-[N-(1-Phosphono-3-[8-(7,9-dioxo-8-azaspiro[4,5]decyl)]propyl)-(S)-leucyl]-(S)-lysine-N-methylamide.

As noted above, numerous inhibitors of matrix metalloproteinases are known. A large number of inhibitors are characterized as hydroxamic acid-based and/or carboxylic acid-based compounds. Typical of such compounds are those described in the following references, all of which are incorporated herein by reference, since all of the disclosed compounds can be used in the method of this invention.

US 4,599,361 (Searle)

US 4,771,038 (ICI)

US 4,996,358 (Roche)

US 4,918,105 (Bellon)

US 5,304,604; US 5,514,677 (British Biotechnology)

US 5,240,958; US 5,310,763; US 5,530,161 (British Biotechnology)

US 5,453,438 (British Biotechnology)

US 5,239,078 (Glycomed)

US 5,183,900 (Glycomed)

US 5,270,326 (Glycomed)

WO 92/17460 (Smith-Kline Beecham)

US 5,300,501 (Celltech)

US 5,304,549 (Roche)

US 5,256,657 (Sterling Winthrop)

US 5,300,674; US 5,412,145 (British Biotechnology)

US 5,387,610; US 5,616,605 (Research Corporation Technologies)

US 5,442,110; US 5,473,100 (Yamanouchi)

US 5,643,908 (Sankyo)

US 5,525,629 (British Biotechnology)

US 5,569,665 (Celltech)

US 5,530,128 (Celltech)

US 5,318,964; US 5,447,929 (Roche)

US 5,643,964; US 5,700,838 (British Biotechnology)

WO 97/27174 (Shionogi)

An especially preferred group of compounds to be employed in the present method are those described in WO 95/35275 and WO 95/35276, both of which are incorporated herein by reference. Typical compounds from within these groups to be employed include:

N-Hydroxy-2-[[(2-(4-methoxy-phenoxy)-ethyl-(toluene-4-sulfonyl)-amino]-acetamide;

N-Hydroxy-2-[(4-phenoxy-ethyl)-toluene-4-sulfonyl) amino]-acetamide;

N-Hydroxy-2-[(4-methoxy-benzenesulfonyl)-nonyl-amino]-acetamide;

2-[-Decyl-(toluene-4-sulfonyl)-amino]-N-hydroxy-acetamide;

2-Benzyl-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide;

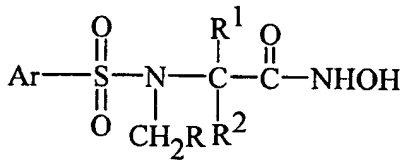
N-Hydroxy-2-[(2-methoxy-benzyl)-(octane-1-sulfonyl)-amino]-acetamide;

2-[(2-Ethoxy-benzyl)-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide;

N-Hydroxy-2-[(naphthalen-2-yl-methyl)-(octane-1-sulfonyl)-amino]-acetamide;

2-[(4-Chloro-benzyl)-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide, and salts, solvates, or hydrates thereof.

Another class of matrix metalloproteinase inhibitors are aryl sulfonamides of the formula



where Ar is carbocyclic or heterocyclic aryl, and R, R^1, and R^2 include hydrogen, alkyl, aryl, heteroaryl, amino, substituted and disubstituted amino. These compounds are disclosed in European Patent Number 0606046, incorporated herein by reference. Specific compounds to be employed in the present method include:

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](isobutyl) amino]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](cyclo-hexylmethyl)amino]-acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](cyclo-hexyl)amino]-acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](phenethyl)amino]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](3-methylbutyl)amino]-acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](sec-butyl)amino]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](tert-butyl)amino]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](4-fluorobenzyl)amino]-acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](4-chlorobenzyl)amino]-acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](isopropyl)-amino]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](4-methylbenzyl)amino]-acetamide;

4-N-Hydroxy-carbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[dimethylaminoacetyl]-piperidine hydrochloride;

4-N-Hydroxy-carbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[3-picolyl]-piperidine dihydrochloride;

4-N-Hydroxy-carbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[carbomethoxymethyl]-piperidine hydrochloride;

4-N-Hydroxy-carbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-piperidine trifluoroacetate;

4-N-Hydroxy-carbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[t-butoxycarbonyl]-piperidine;

4-N-Hydroxycarbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[methylsulfonyl]-piperidine;

N-Hydroxycarbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)-amino]-1-[4-picoly]-piperidine hydrochloride;

N-Hydroxycarbamoyl]-4-[[4-methoxybenzene-sulfonyl(benzyl)amino]-1-[morpholinocarbonyl]-piperidine hydrochloride; and

N-(t-Butyloxy)-2-[[4-methoxybenzenesulfonyl (benzyl)amino]-2-[2-(4-morpholino)ethyl]acetamide.

The following compounds are prepared similarly to Example 7:

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](isobutyl)-amino-2-(2-(4-morpholino)ethyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](2-picoly)-amino-2-(2-(4-morpholino)ethyl]acetamide dihydro-chloride;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](3-picolyl)amino]-2-[2-(4-morpholino)ethyl]acetamide dihydrochloride;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](2-methyl-thiazol-4-ylmethyl)amino]-2-[2-(4-morpholino) ethyl]acetamide dihydrochloride;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl]benzyl)amino]-2-[2-(4-thiomorpholino]ethyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](benzyl)amino]-2-[2-(4-methylthiazol-4-ylmethyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl(benzyl)amino]-2-[(6-chloropiperonyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl(benzyl)amino]-2-[(1-pyrazolyl)methyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl(3-picolyl)amino]-2-[3-picolyl]acetamide;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl(benzyl)-amino]-2-[(1-methyl-4-imidazolyl)methyl]acetamide hydrochloride;

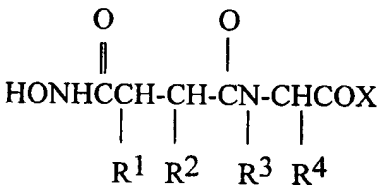
N-Hydroxy-2-[[4-methoxybenzenesulfonyl(isobutyl)amino]-2-[(1-methyl-4-imidazolyl)methyl]acetamide hydrochloride;

N-Hydroxy-2-[[4-methoxybenzenesulfonyl](3-picolyl)amino]-2-[(1-methyl-4-imidazolyl)methyl]acetamide hydrochloride;

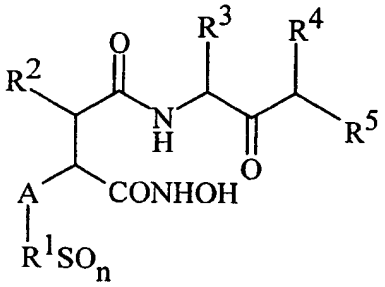
N-Hydroxy-2-[[4-methoxybenzenesulfonyl(2-picolyl)amino]-2-[(1-methyl-4-imidazolyl)methyl]-acetamide hydrochloride; and

N-Hydroxy-2-[[4-methoxybenzenesulfonyl] (2-methylthiazol-4-ylmethyl)amino-2-[(1-methyl-4-imidazolyl)methyl]acetamide hydrochloride.

Another group of small peptide matrix metalloproteinase inhibitors are described in United States Patent Numbers 5,270,326, 5,530,161, 5,525,629, and 5,304,604 (incorporated herein by reference). The compounds are hydroxamic acids defined by the formula



and



where R^1, R^2, R^3, and R^4 can be hydrogen or alkyl and X is OR^5 or NHR^5 where R^5 includes hydrogen, alkyl and aryl, A includes alkyl, and n is 0 to 2. Typical compounds to be employed in the instant method include the following:

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-D-tryptophan methylamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-N-methyl-L-tryptophan methylamide;

N-[2-Isobutyl-3-(N-hydroxycarbonylamido)-propanoyl]-L-3-(2-naphthyl)-alanine methylamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-L-tryptophan 2-hydroxyethylamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-L-tryptophan amylamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-L-tryptophan piperidinamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl-L-tryptophan dodecylamide;

N-[2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-L-tryptophan(S)-methylbenzylamide;

N-[L-2-Isobutyl-3-(N′-hydroxycarbonylamido)-propanoyl]-L-tryptophan(6-phenylmethoxycarbonyl-amino-hexyl-1)amide;

2S-Hydroxy-3R-[1S-(3-methoxy-2,2-dimethyl-propylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-6-(4-chloro)phenyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-octanohydroxamic acid;

2S-Hydroxy-3R-[1S-(pyridin-2-ylmethylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(pyridin-3-ylmethylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(pyridin-4-ylmethylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-4-methoxy-butanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-4-benzyloxy-butanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-4-benzylthio-butanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-buten-3-ylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(*tert*-butylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(N,N-dimethyl-carbamoyl)-2,2-dimethyl-propylcarbamoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(3-hydroxy-2,2-dimethyl-propylcarbamoyl)-2,2-dimethyl-propylcarbanoyl]-5-methyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-propylcarbamoyl]-6-phenyl-hexanohydroxamic acid;

2S-Hydroxy-3R-[1S-(methylcarbamoyl)-2,2-dimethyl-butylcarbamoyl]-5-methyl-hexanohydroxamic acid;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-hydroxyethyl)-amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalaninyl-proline;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-hydroxyethyl)-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalaninyl-D-prolinol;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalaninyl-L-prolinol;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(5-N-methyl-pentylcarboxamide)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-ethylthioethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-methoxyethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-N-acetylethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide sodium salt;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-acetoxyethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-methyl-N-(2-hydroxyethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-(2-hydroxyethyl)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalaninyl-D-prolinol;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide sodium salt;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-(3-(2-pyrrolidone)propyl)amide or a salt thereof;

N^2-[4-(N-Hydroxyamino)-3S-(4-hydroxyphenylthiomethyl)-2R-isobutylsuccinyl]-N^6-*tert*-butyloxycarbonyl-L-lysine-N^1-methylamide;

N^2-[4-(N-Hydroxyamino)-3S-(4-hydroxyphenylthiomethyl)-2R-isobutylsuccinyl]-N^6-*tert*-butyloxycarbonyl-N^6-(4-hydroxyphenylthiomethyl)-L-lysine-N^1-methylamide;

N^2-[4-(N-Hydroxyamino)-3S-(2-thienylthiomethyl)-2R-isobutylsuccinyl]-N^6-*tert*-butyloxycarbonyl-L-lysine-N^1-methylamide;

N^2-[4-(N-Hydroxyamino)-3S-(4-hydroxyphenylthiomethyl)-2R-isobutylsuccinyl]-O-*tert*-butyl-L-threonine-N^1-methylamide;

N^2-[4-(N-Hydroxyamino)-3S-(4-hydroxyphenylthiomethyl)-2R-isobutylsuccinyl]-L-glutamine-N^1,N^5-dimethylamide;

N^2-[4-(N-Hydroxyamino)-3S-(4-hydroxyphenylsulphonylmethyl)-2R-isobutylsuccinyl]-N^6-acetyl-L-lysine-N^1-methylamide;

3R-(3-Methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-2S-2-propenyl-hexanohydroxamic acid;

3R-(1S-Methylcarbamoyl-2-thien-2-yl-ethylcarbamoyl)-5-methyl-2S-2-propenyl-hexanohydroxamic acid;

3R-(3-Methyl-1S-methylcarbamoyl-butylcarbamoyl)-5-methyl-2S-2-propenyl-hexanohydroxamic acid;

2S-[1S-Methylcarbamoyl-2-oxadiazol-5-yl-ethylcarbamoyl)-5-methyl-2S-2-propenyl-hexanohydroxamic acid;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxylic acid)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxy-N-methylamide)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxy-beta-alanine)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxyglycine)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxy-N-benzylamide)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-cyano)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-acetamido)-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-(4-oxymethylcarboxamide)-henylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethylsuccinyl]-L-(4-N-acetylamino)-henylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethylsuccinyl]-L-(4-N-methylsuccinylamide)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-aminophenylthiomethyl)-succinyl]-L-(4-N-(methylsuccinylamide)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-aminophenylthiomethylsuccinyl]-L-(4-N-(4-(4-oxobutanoic acid)-aminophenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-hydroxyphenylthiomethyl)-succinyl]-L-(4-N-methylsuccinylamido)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-hydroxyphenylthiomethyl)-succinyl]-L-(4-N-(4-(4-oxobutanoic acid)aminophenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethyl)-succinyl]-L-(4-oxymethylcarboxymethyl)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethyl)-succinyl]-L-(4-N-(oxymethylcarboxylic acid)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethyl)-succinyl]-L-4-oxymethylcarboxyglycyl methyl ester)-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2-thienylthiomethyl)-succinyl]-L-4-oxymethylcarboxyglycine)phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl-succinyl]-L-4-(oxymethylcarboxyglycyl methyl ester)-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methyl)-succinyl]-L-4-(oxymethylcarboxyglycine)-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-4-oxymethylnitrile)-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-3-(1-(2-methyloxycarbonyl)-ethyl)-4-methoxyphenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-3-(hydroxymethyl)-4-methoxyphenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-3-methyl-4-methoxyphenylalanine-N-methylamide;

2-[Benzyl-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide;

N-Hydroxy-2-[(2-methoxy-benzyl)-(octane-1-sulfonyl)-amino]-acetamide;

2-[(2-Ethoxy-benzyl)-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide;

N-Hydroxy-2-[(naphthalen-2-yl-methyl)-(octane-1-sulfonyl)-amino]-acetamide;

2-[(4-Chloro-benzyl)-(octane-1-sulfonyl)-amino]-N-hydroxy-acetamide;

N^2-[3S-Hydroxy-4-(N-hydroxyamino)-2R-isobutylsuccinyl]-L-leucine-N^1-methylamide;

N^2-[3S-Hydroxy-4-(N-hydroxyamino)-2R-isobutylsuccinyl)]-5-methyl-L-glutamic acid-N^1-methylamide;

N^2-[3S-Hydroxy-4-(N-hydroxyamino)-2R-isobutylsuccinyl)]-L-phenylalanine-N^1-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(thienylthiomethyl)succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-phenylthiomethyl)succinyl]-L-phenylalanine-N-methylamide;

2S-(4-Methoxyphenylsulfanylmethyl)-3R-(2-phenyl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(3-Chlorophenylsulfanylmethyl)-3R-(2-phenyl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Phenylsulfanylmethyl)-3R-(2-phenyl-1S-(pyrid-3-ylmethylcarbamoyl)-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(3-Methylphenylsulfanylmethyl)-3R-(2-phenyl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Thien-2-ylsulfanylmethyl)-3R-(2-(4-carboxymethoxyphenyl)-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Thien-2-ylsulfanylmethyl)-3R-(2-phenyl-1S-(pyrid-3-ylmethylcarbamoyl)-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxyphenylsulfanylmethyl)-3R-(2-phenyl-1S-(pyrid-3-ylmethylcarbamoyl)-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Thien-2-ylsulfanylmethyl)-3R-(2-naph-2-yl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxyphenylsulfanylmethyl)-3R-(2R-hydroxy-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxyphenylsulfanylmethyl)-3R-(5-acetamido-1S-methylcarbamoyl-pentylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxyphenylsulfanylmethyl)-3R-(3-[1,1-dimethylethoxycarbonyl]-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Thien-2-ylsulfonylmethyl)-3R-(2-phenyl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

3S-(2-[4-Acetamido-phenyl]-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Phthalimido-butyl)-3R-(3-methyl-1S-ethoxycarbonylmethylcarbamoyl-butylcarbamoyl)-5-methyl-hexanohydroxamic acid;

3R-(2-[4-Methoxy-phenyl]-1S-methylcarbamoyl-ethylcarbamoyl)-2S,5-dimethyl-hexanohydroxamic acid;

3R-(2-Phenyl-1S-[2-oxo-pyrolid-1-yl]-propylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

3R-(2-[4-Methoxy-phenyl]-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

3R-(2-Phenyl-1S-[pyrid-3-ylmethylcarbamoyl]-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

3R-(2,2-Dimethyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

Isobutylmalonoyl-L-alanine-furfurylamide hydroxamate;

2-Isobutyl-3-carbonyl-3'-(4-acetylaniline)propionic acid;

N-Benzyloxycarbonyl-α-phosphonoglycyl-L-alanine furfurylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(phenylthiomethyl)succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-methoxyphenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-hydroxyphenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(2,4-dimethylphenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(3-bromophenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(3-chlorophenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(3-methylphenylthiomethyl)-succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-(4-(N-acetyl)-amino-phenylthiomethyl)succinyl]-L-phenylalanine-N-methylamide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-phenylsulphinylmethylsuccinyl]-L-phenylalanine-N-methylamide;

3R-(3-Methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-2S-phenylsulfanylmethyl- hexanohydroxamic acid;

3R-(3-Methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-2S-(thien-2-ylsulfanylmethyl)-hexanohydroxamic acid;

2S-(4-Methoxy-phenylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Amino-phenylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Ethylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Acetylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(Benzylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(*tert*-Butylsulfanylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-Thiomethyl-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxy-phenylsulfanylmethyl)-3R-(2-*tert*-butoxycarbonyl-1S-methylcarbamoyl-ethylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxy-phenylsulphinylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

2S-(4-Hydroxy-phenylsulphonylmethyl)-3R-(3-methoxycarbonyl-1S-methylcarbamoyl-propylcarbamoyl)-5-methyl-hexanohydroxamic acid;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-[1-(2-aminoethyl)-pyrrolidine]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-[1-(3-aminopropyl)-2(RS)-methylpiperidine]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-[2-(2-aminoethyl)-1-methylpyrrole]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(3-aminomethylpyridine)amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(2-aminomethylpyridine)amide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-phenylalanine-N-(4-aminomethylpyridine)amide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-phenylalanine-N-(1-(3-aminopropyl)-imidazole)amide;

[4-(N-Hydroxyamino)-2(RS)-isobutylsuccinyl]-L-phenylalanine-N-(2-aminomethylbenzimdazole)amide;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-methylsuccinyl]-L-phenylalanine-N-[4-(2-aminoethyl)-morpholino]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-[4-(2-aminoethyl)-morpholine]amide;

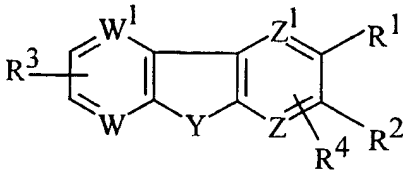
[4-(N-Hydroxyamino)-2(R,S)-isobutylsuccinyl]-L-phenylalanine-N-[2-(2-aminoethyl)-pyridine]amide;

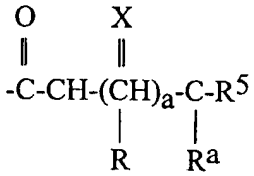
[4-(N-Hydroxyamino)-2(R,S)-isobutylsuccinyl]-L-phenylalanine-N-[4-(2-aminopropyl)-morpholine]amide;

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-(3-aminomethylpyridine)amide hydrochloride; and

[4-(N-Hydroxyamino)-2R-isobutylsuccinyl]-L-phenylalanine-N-[4-(2-aminoethyl)-morpholine]amide hydrochloride.

In a preferred embodiment, tricyclic butyric acid derivatives which are inhibitors of matrix metalloprotienases are employed in the instant invention. A preferred group of tricyclic butyric acid derivatives are defined by the formula:



wherein one of R^1 or R^2 s 

wherein X is O,

N-OR^6 wherein R^6 is hydrogen,

$-(CH_2)_n$-aryl wherein n is zero or an integer of 1 to 5,

alkyl, or

$-(CH_2)_n$-cycloalkyl wherein n is as defined above, or

$N\text{-}N\text{-}R^6$ wherein R^6 and R^{6a} are each the same or different and
R_{6a}
each is as defined above for R^6;

R and R^a are each the same or different and each is hydrogen,

$-(CH_2)_n$-aryl wherein n is as defined above,

$-(CH_2)_n$-heteroaryl wherein n is as defined above,

$-(CH_2)_p-R^7-(CH_2)_q$-aryl wherein R^7 is O or S and p or q is each zero or an integer of 1 to 5 and the sum of p + q equals an integer of 5,

$-(CH_2)_p-R^7-(CH_2)_q$-heteroaryl wherein p, q, and R^7 are as defined above,

alkyl,

$-(CH_2)_n$-cycloalkyl wherein n is as defined above, or

$-(CH_2)_r-NH_2$ wherein r is an integer of 1 to 9;

a is zero or an integer of 1 to 3;

R^5 is OH,

OR^6 wherein R^6 is as defined above,

NR^6 wherein R^6 and R^{6a} are each
R^{6a}
the same or different and are as defined above for R^6, or

$NH\text{-}OR^6$ wherein R^6 is as defined above;

R^3 and R^4 are each the same or different and each is hydrogen,

alkyl,

NO_2,

halogen,

OR^6 wherein R^6 is as defined above,

CN,

CO_2R^6 wherein R^6 is as defined above,

SO_3R^6 wherein R^6 is as defined above,

CHO,

$-\overset{\overset{O}{\|}}{C}-R$ wherein R is as defined above,

$-\overset{\overset{O}{\|}}{C}-N(R^{6a})-R^{6}$ wherein R^6 and R^{6a} are each the same or different and are as defined above for R^6, or

$-(CH_2)_n-N(R^{6a})-R^{6}$ wherein R^6 and R^{6a} are each the same or different and are as defined above for R^6;

W, W^1, Z, and Z^1 are each the same or different and each is CR^3 wherein R^3 is as defined above, or

N providing only one of W or W^1 is

N and/or only one of Z or Z^1 is N; and

Y is $-N(R)-$ wherein R is as defined above,

$-O-$,

$-S-(O)_m-$ wherein m is zero or an integer of 1 or 2,

$-CH_2-$,

$-\overset{\overset{O}{|}}{C}-$,

$-\overset{\overset{N-OR^{6}}{|}}{C}-$ wherein R^6 is as defined above,

$-\overset{\overset{OR^{6}}{|}}{CH}-$ wherein R^6 is as defined above,

-C- wherein R^6 and R^{6a} are the same or different and are as defined
|
N-N-R^6
|
R^{6a}

above for R^6,

-C-N- wherein R^6 is as defined above,
‖ |
O R^6

-N–C- wherein R^6 is as defined above,
‖ |
R^6O

-C-O-,
‖
O

-O-C-,
‖
O

$-CH_2-O-$,

$-O-CH_2-$,

$-CH_2-S(O)_m-$ wherein m is as defined above,

$-S(O)_m-CH_2-$ wherein m is as defined above,

$-CH_2-N-$ wherein R^6 is as defined above,
|
R^6

$-N-CH_2-$ wherein R^6 is as defined above,
|
R^6

-CH=N-, or

-N=CH-;

with the proviso that when X is O, and R^5 is not NH-OR^6, at least one of R or R^a is not hydrogen; and corresponding isomers thereof; or a pharmaceutically acceptable salt thereof.

Typical compounds from this class include:

4-Dibenzofuran-2-yl-4-hydroxyimino-butyric acid;

2-(2-Dibenzofuran-2-yl-2-hydroxyimino-ethyl)-4-methyl-pentanoic acid;

2-(2-Dibenzofuran-2-yl-2-hydroxyimino-ethyl)-5-phenyl-pentanoic acid;

4-Dibenzofuran-2-yl-4-hydroxyimino-2-phenethyl-butyric acid;

5-(4-Chloro-phenyl)-2-(2-dibenzofuran-2-yl-2-hydroxyimino-ethyl)-pentanoic acid;

2-(2-Dibenzofuran-2-yl-2-hydroxyimino-ethyl)-5-(4-fluoro-phenyl)-pentanoic acid;

2-(2-Dibenzofuran-2-yl-2-hydroxyimino-ethyl)-5-(4-methoxy-phenyl)-pentanoic acid;

2-(2-Dibenzofuran-2-yl-2-hydroxyimino-ethyl)-5-p-tolyl-pentanoic acid;

3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-5-methyl-hexanoic acid;

3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-6-phenyl-hexanoic acid;

3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-5-phenyl-pentanoic acid;

6-(4-Chloro-phenyl)-3-(dibenzofuran-2-yl-hydroxyimino-methyl)-hexanoic acid;

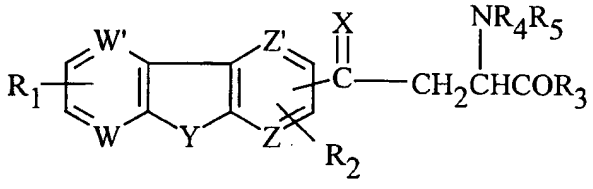
3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-6-(4-fluoro-phenyl)-hexanoic acid;

3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-6-(4-methoxyphenyl)-hexanoic acid; and

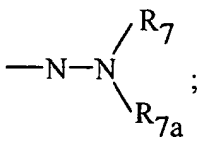
3-(Dibenzofuran-2-yl-hydroxyimino-methyl)-6-p-tolyl-hexanoic acid; and corresponding isomers thereof;

or a pharmaceutically acceptable salt thereof.

Tricyclic butyric acids having an α-amino substituent are defined by the formula:



wherein:

X is O, NOR_9, S, OH, SH, or  ;

R_7 and R_{7a} independently are

hydrogen,

C_1-C_{20} alkyl or substituted C_1-C_{20} alkyl,

$(CH_2)_{0-6}$-aryl,

$(CH_2)_{0-6}$-heteroaryl, or

$(CH_2)_{0-6}$-cycloalkyl;

R_1 and R_2 independently are

hydrogen,

C_1-C_{20} alkyl or substituted C_1-C_{20} alkyl,

halo,

NO_2,

CN,

CHO,

COR_6,

$COOR_6$,

SO_3R_6,

OR_6,

$CONR_4R_5$,

$(CH_2)_{0-6}$-aryl,

$(CH_2)_{0-6}$-heteroaryl, or

$(CH_2)_{0-6}$-cycloalkyl;

R_6 is hydrogen,

C_1-C_{20} alkyl or substituted C_1-C_{20} alkyl;

aryl is phenyl or substituted phenyl;

R_3 is hydroxy,

O-C_1-C_{20} alkyl or substituted O-C_1-C_{20} alkyl,

O-$(CH_2)_{1-3}$ aryl, or

$NHOR_6$;

R_4 and R_5 independently are hydrogen,

C_1-C_{20} alkyl or substituted C_1-C_{20} alkyl,

$(CH_2)_{0-6}$-aryl,

$(CH_2)_{0-6}$-heteroaryl; or one of R_4 and R_5 is hydrogen and the other is:

COR_8,

CSR_8,

$CONR_8R_9$,

$CSNR_8R_9$,

$COOR_8$,

$COSR_8$,

$COCHR_8$,
|
NR_1R_2

$CON\text{-}CONR_8R_9$,
|
R_1

$CON\text{-}COOR_8$,
|
R_1

$CON\text{-}COSR_8$, or
|
R_1

$CON\text{-}SO_2NR_8R_9$;
|
R_1

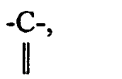
$CON\text{-}SO_3R_8$;
|
R_1

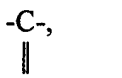
Y is -N-,
|
R_1

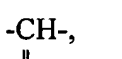
-O-,

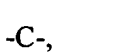
$-S(O)_{0,\ 1\ or\ 2}$,

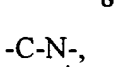
$-CH_2$-,

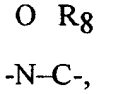


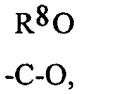










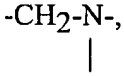


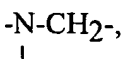
$-CH_2-O-$,

$-O-CH_2-$,

$-CH_2S(O)_{0, 1 \text{ or } 2}$,

$-S(O)_{0, 1 \text{ or } 2}-CH_2-$,





-CH=N, or

-N=CH-;

R_8 and R_9 independently are

hydrogen,

C_1-C_{20} alkyl or substituted C_1-C_{20} alkyl,

$(CH_2)_{0-6}$-aryl,

$(CH_2)_{0-6}$-heteroaryl, or

$(CH_2)_{0-6}$-cycloalkyl;

W, W^1, Z, and Z^1 independently are CR_1 or N;

and the pharmaceutically acceptable salts, isomers, stereoisomers, and solvates thereof.

Specific examples of compounds to be employed in the present method include:

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(2,2,2-trifluoroacetylamino)-butyric acid;

(R)-4-Dibenzofuran-2-yl-4-oxo-2-(2,2,2-trifluoroacetylamino)-butyric acid;

(S)-2-Amino-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-2-Acetylamino-4-dibenzofuran-2-yl-4-oxo-butyric;

(S)-4-Dibenzofuran-2-yl-2-[3-(2,6-diisopropyl-phenyl)-ureido]-4-oxo-butyric acid;

(S)-2-Benzoylamino-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-phenylacetylamino-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(3-phenyl-propionylamino)-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(7-phenyl-heptanoylamino)-butyric acid;

(S)-2-[(Biphenyl-4-carbonyl)-amino]-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(dodecanoylamino)-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(dodecanoyl-amino)-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(2,2,2-trifluoroacetylamino)-butyric acid;

(R)-4-Dibenzofuran-2-yl-4-oxo-2-(2,2,2-trifluoroacetylamino)-butyric acid;

(S)-2-Amino-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-2-Acetylamino-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-4-Dibenzofuran-2-yl-2-[3-(2,6-diisopropyl-phenyl)-ureido]-4-oxo-butyric acid;

(S)-2-Benzoylamino-4-dibenzofuran-2-yl-4-oxo-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-phenylacetylamino-butyric acid;

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(3-phenyl-propionylamino)-butyric acid;

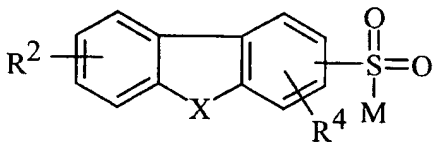
(S)-4-Dibenzofuran-2-yl-4-oxo-2-(7-phenyl-heptanoylamino)-butyric acid;

(S)-2-[(Biphenyl-4-carbonyl)-amino]-4-dibenzofuran-2-yl-4-oxo-butyric acid;

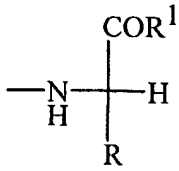
(S)-4-Dibenzofuran-2-yl-4-oxo-2-(octanoylamino)-butyric acid; and

(S)-4-Dibenzofuran-2-yl-4-oxo-2-(dodecanoylamino)-butyric acid.

Tricyclic sulfonamide matrix metalloproteinase inhibitors include compounds of the formula



wherein M is a natural (L) alpha amino acid derivative having the structure



X is O, S, $S(O)_n$, CH_2, CO, or NH;

R is a side chain of a natural alpha amino acid;

R^1 is C_1-C_5 alkoxy, hydroxy, or $-NHOR^5$;

R^2 and R^4 are independently hydrogen, -C_1-C_5 alkyl, $-NO_2$, halogen, $-OR^5$, -CN, $-CO_2R^5$, $-SO_3R^5$,-CHO, $-COR^5$, $-CONR^5R^6$, $-(CH_2)_nNR^5R^6$, $-CF_3$, or $-NHCOR^5$;

each R^5 and R^6 are independently hydrogen or C_1-C_5 alkyl; and

n is 0 to 2, and the pharmaceutically acceptable salts, ester, amides, and prodrugs thereof.

Specific compounds from this class to be employed include:

(L)-2-(Dibenzofuran-2-sulfonylamino)-4-methyl-pentanoic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-pentanoic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-phenyl-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-butyric acid;

(Dibenzofuran-2-sulfonylamino)-acetic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-succinic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-tritylsulfanyl-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-mercapto-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-pentanoic acid hydroxyamide;

(L)-2-(Dibenzofuran-2-sulfonylamino)-4-methyl-pentanoic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-pentanoic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-phenyl-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-butyric acid;

(Dibenzofuran-2-sulfonylamino)-acetic acid;

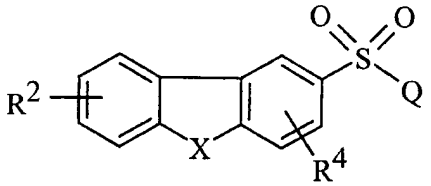
(L)-2-(Dibenzofuran-2-sulfonylamino)-succinic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-tritylsulfanyl-propionic acid;

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-mercapto-propionic acid; and

(L)-2-(Dibenzofuran-2-sulfonylamino)-3-methyl-pentanoic acid hydroxyamide.

Additional tricyclic sulfonamides are defined by the formula:



wherein Q is an un-natural amino acid;

X is O, S, $S(O)_n$, CH_2, CO, or NH;

R^2 and R^4 are independently hydrogen, C_1-C_5 alkyl, $-NO_2$, halogen, $-OR^5$, -CN, $-CO_2R^5$, $-SO_3R^5$, -CHO, $-COR^5$, $-CONR^5R^6$, $-(CH_2)_nNR^5R^6$, $-CF_3$, or $-NHCOR^5$;

each R^5 and R^6 are independently hydrogen or C_1-C_5 alkyl; and

n is 0 to 2, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

Specific examples of such compounds include:

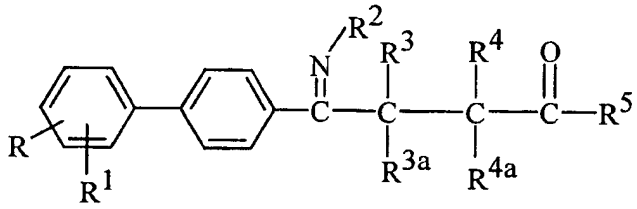
(S)-2-(Dibenzofuran-2-sulfonylamino)-4-phenyl-butyric acid;

2 (S)-3-[(Dibenzofuran-2-sulfonylamino)-methyl]-5-methyl-hexanoic acid;

(S)-2-(Dibenzofuran-2-sulfonylamino)-4-phenyl-butyric acid; and

2 (S)-3-[(Dibenzofuran-2-sulfonylamino)-methyl]-5-methyl-hexanoic acid.

Another general class of matrix metalloproteinase inhibitors, which are useful to treat and prevent heart failure and ventricular dilatation, are biphenyl butyric acid derivatives, including compounds of the formula:



wherein R and R^1 are the same or different and are

hydrogen,

alkyl,

halogen,

nitro,

cyano,

trifluoromethyl,

$-OR^6$ wherein R^6 is hydrogen,

alkyl,

aryl,

arylalkyl,

heteroaryl, or

cycloalkyl,

$-N(R^6)(R^{6a})$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^6,

-O-C-R^6 wherein R^6 is as defined above,

-NH-C-R^6 wherein R^6 is as defined above,

-S-C-R^6 wherein R^6 is as defined above,

-SR^6 wherein R^6 is as defined above,

-C-R^6 wherein R^6 is as defined above,

-CH_2-OR^6 wherein R^6 is as defined above,

-CH_2-N-R^6 wherein R^6 and R^{6a} are the same or different and are as

defined above for R^6,

-C-N-R^6 wherein R^6 and R^{6a} are the same or different and are as

defined above for R^6,

-S-R^6 wherein R^6 is as defined above,

cycloalkyl, or

heteroaryl, with the proviso that R and R^1 are not both hydrogen;

R^2 is -OR^6 wherein R^6 is as defined above, or

-N-R^6 wherein R^6 and R^{6a} are the same or different and are as

defined above for R^6;

R^3, R^{3a}, R^4, and R^{4a} are the same or different and are

hydrogen,

fluorine,

alkyl,

$-(CH_2)_n$-aryl wherein n is an integer from 1 to 6,

$-(CH_2)_n$-heteroaryl wherein n is as defined above,

$-(CH_2)_n$-cycloalkyl wherein n is as defined above,

$-(CH_2)_p$-X-$(CH_2)_q$-aryl wherein X is O, S, SO, SO_2, or NH, and p and q are each zero or an integer of 1 to 6, and the sum of p + q is not greater than six,

$-(CH_2)_p$-X-$(CH_2)_q$-heteroaryl wherein X, p, and q are as defined above,

or

$-(CH_2)_n-R^7$ wherein R^7 is

N-phthalimido,

N-2,3-naphthyimido,

$-OR^6$ wherein R^6 is as defined above,

$-N(R^{6a})-R^6$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^6,

$-SR^6$ where R^6 is as defined above,

$-S(=O)-R^6$ wherein R^6 is as defined above,

$-S(=O)_2-R^6$ wherein R^6 is as defined above,

$-O-C(=O)-R^6$ wherein R^6 is as defined above,

-N-C-R^6 wherein R^6 and R^{6a} are the same or different and are as

defined above for R^6,

-S-C-R^6 wherein R^6 is as defined above,

-C-R^6 wherein R^6 is as defined above,

-C-OR^6 wherein R^6 is as defined above, or

-C-N-R^6 wherein R^6 and R^{6a} are the same or different and are as

defined above for R^6, and

n is as defined above;

R^5 is OH or SH; with the proviso that R^3, R^{3a}, R^4, and R^{4a} are hydrogen or at least one of R^3, R^{3a}, R^4, or R^{4a} is fluorine; and corresponding isomers thereof; or a pharmaceutically acceptable salt thereof.

Typical compounds from this class that are routinely utilized to treat atherosclerosis include:

4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(4′-Bromo-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-4-(dimethylhydrazono)-butyric acid;

4-(4′-Fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxy-butyric acid;

4-(4′-Bromo-2′-fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-3-fluoro-4-oxo-butyric acid;

4-(2′,4′-Dichloro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(2′,4′-Difluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(3-phenylpropyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(2-phenylethyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(3-phthalimidopropyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(phenylthiomethyl)-butyric acid;

4-(4′-Chloro-2′-fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-Hydroxyimino-4-(4′-trifluoromethyl-biphenyl-4-yl)-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-4-methoxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2-fluoro-2-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(1H-indol-3-yl)methyl-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-methyl-butyric acid;

(±)-2-[2-(4′-Chloro-biphenyl-4-yl)-2-hydroxyiminoethyl]-2-fluoro-6-phenyl-hexanoic acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2-fluoro-2-[2-(1,3-dioxo-1,3-dihydro-benzo[F]isoindol-2-yl)-ethyl]-4-hydroxyimino-butyric acid;

(±)-2-[2-(4′-Chloro-biphenyl-4-yl)-2-hydroxyiminoethyl]-6-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-2-fluoro-hexanoic acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-[2-(phenyl-ethylcarbamoyl)-ethyl]-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-3,3-difluoro-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-3,3-dimethyl-2-fluoro-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2,2-dimethyl-3-fluoro-4-hydroxyimino-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-2,2-difluoro-4-hydroxyimino-butyric acid; and

4-(4′-Chloro-biphenyl-4-yl)-2,2,3,3-tetrafluoro-4-hydroxyimino-butyric acid.

A compound selected from the group consisting of:

4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(4′-Bromo-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-4-(dimethylhydrazono)-butyric acid;

4-(4′-Fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxy-butyric acid;

4-(4′-Bromo-2′-fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-3-fluoro-4-oxo-butyric acid;

4-(2′,4′-Dichloro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-(2′,4′-Difluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(3-phenylpropyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(2-phenylethyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(3-phthalimidopropyl)-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(phenylthiomethyl)-butyric acid;

4-(4′-Chloro-2′-fluoro-biphenyl-4-yl)-4-hydroxyimino-butyric acid;

4-Hydroxyimino-4-(4′-trifluoromethyl-biphenyl-4-yl)-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-4-methoxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2-fluoro-2-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-(1H-indol-3-yl)methyl-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-methyl-butyric acid;

(±)-2-[2-(4′-Chloro-biphenyl-4-yl)-2-hydroxyiminoethyl]-2-fluoro-6-phenyl-hexanoic acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2-fluoro-2-[2-(1,3-dioxo-1,3-dihydro-benzo[F]isoindol-2-yl)-ethyl]-4-hydroxyimino-butyric acid;

(±)-2-[2-(4′-Chloro-biphenyl-4-yl)-2-hydroxyiminoethyl]-6-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-2-fluoro-hexanoic acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-4-hydroxyimino-2-fluoro-2-[2-(phenyl-ethylcarbamoyl)-ethyl]-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-3,3-difluoro-4-hydroxyimino-butyric acid;

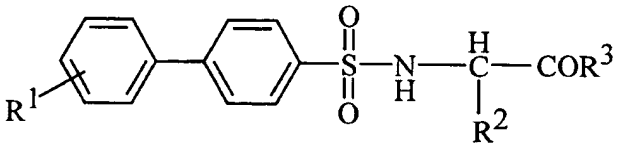
(±)-4-(4′-Chloro-biphenyl-4-yl)-3,3-dimethyl-2-fluoro-4-hydroxyimino-butyric acid;

(±)-4-(4′-Chloro-biphenyl-4-yl)-2,2-dimethyl-3-fluoro-4-hydroxyimino-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-2,2-difluoro-4-hydroxyimino-butyric acid; and

4-(4′-Chloro-biphenyl-4-yl)-2,2,3,3-tetrafluoro-4-hydroxyimino-butyric acid.

Biphenyl sulfonamides are also particularly good in the present method. Such compounds include those of the formula:



wherein:

R^1 is C_1-C_6 alkyl, halo, nitro, NR^4R^5, cyano, OR^4, and $COOR^4$;

R^2 is C_1-C_6 alkyl, optionally substituted by phenyl, substituted phenyl, NR^4R^5, OR^6, carboxy, carboxamido, H_2N-C(=NH)-NH-, thio, methylthio, indole, imidazole, phthalimido, phenyl, and substituted phenyl;

R^3 is OH, OC_1-C_6 alkyl, or NHOH;

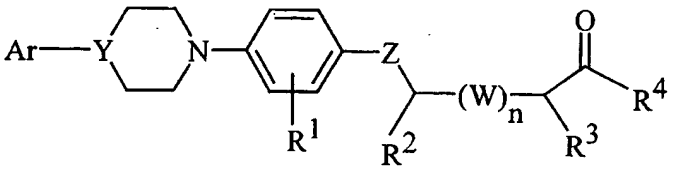
R^4 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 alkanoyl;

R^5 is hydrogen or C_1-C_6 alkyl; and

R^6 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkanoyl, phenyl, or substituted phenyl.

Specific compounds which can be employed include a compound of the above formula wherein R^1 is at the 4′ position.

Another class of matrix metalloproteinase inhibitors useful in the present method are the heterocyclic substituted phenyl butyric acid derivatives, for example those defined by the formula:



Ar is selected from phenyl,

phenyl substituted with

alkyl,

NO_2,

halogen,

OR^5 wherein R^5 is hydrogen or alkyl,

CN,

CO_2R^5 wherein R^5 is as defined above,

SO_3R^5 wherein R^5 is as defined above,

CHO,

COR^5 wherein R^5 is as defined above,

$CONHR^5$ wherein R^5 is as defined above, or

$NHCOR^5$ wherein R^5 is as defined above,

2-naphthyl, or

heteroaryl;

R^1 is selected from hydrogen,

methyl,

ethyl,

NO_2,

halogen,

OR^5 wherein R^5 is as defined above,

CN,

CO_2R^5 wherein R^5 is as defined above,

SO_3R^5 wherein R^5 is as defined above,

CHO, or

COR^5 wherein R^5 is as defined above;

R^2 and R^3 are the same or different and independently selected from hydrogen, alkyl,

$-(CH_2)_v$-aryl wherein v is an integer from 1 to 5,

$-(CH_2)_v$-heteroaryl wherein v is as defined above,

$-(CH_2)_v$-cycloalkyl wherein v is as defined above,

$-(CH_2)_p$-X-$(CH_2)_q$-aryl wherein X is O or S and p and q is each zero or an integer of 1 to 5, and the sum of p + q is not greater than an integer of 5,

$-(CH_2)_p$-X-$(CH_2)_q$-heteroaryl wherein X, p, and q are as defined above,

$-(CH_2)_tNR^6R^{6a}$, wherein t is zero or an integer of from 1 to 9 and R^6 and R^{6a} are each the same or different and are as defined above for R^5,

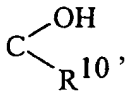
$-(CH_2)_vSR^5$, wherein v and R^5 are as defined above,

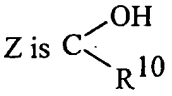
$-(CH_2)_vCO_2R^5$, wherein v and R^5 are as defined above, or

$-(CH_2)_vCONR^6R^{6a}$, wherein R^6 and R^{6a} are the same or different and are as defined above for R^5 and v is as defined above;

R^3 is additionally $-(CH_2)_rR^7$ wherein r is an integer from 1 to 5 and R^7 is 1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl, or 1,3,-dihydro-1,3-dioxo-benzo[f]isoindol-2-yl;

Y is CH or N;

Z is  ,

wherein R^{10} is as defined above for R^2 and R^3, and is independently the same or different from R^2 and R^3 provided that when Z is  , then R^4 must be OH,

C=O,

$C=NOR^5$ wherein R^5 is as defined above, or

$C=N-NR^6R^{6a}$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^5;

W is $-CHR^5$ wherein R^5 is as defined above;

n is zero or an integer of 1;

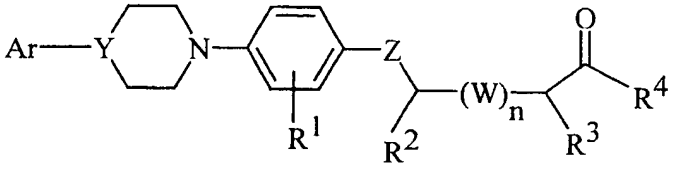
R^4 is OH,

NR^6R^{6a} wherein R^6 and R^{6a} are the same or different and are as defined above for R^5, when R^4 is NR^6R^{6a} then Z must be C=O or

$NHOR^9$ wherein R^9 is hydrogen, alkyl, or benzyl;

and corresponding isomers thereof; or a pharmaceutically acceptable salt thereof.

Especially preferred MMP inhibitors have the formula



Ar is selected from phenyl,

phenyl substituted with

alkyl,

NO_2,

halogen,

OR^5 wherein R^5 is hydrogen or alkyl,

CN,

CO_2R^5 wherein R^5 is as defined above,

SO_3R^5 wherein R^5 is as defined above,

CHO,

COR^5 wherein R^5 is as defined above,

$CONHR^5$ wherein R^5 is as defined above, or

$NHCOR^5$ wherein R^5 is as defined above,

2-naphthyl, or

heteroaryl;

R^1 is selected from hydrogen,

methyl,

ethyl,

NO_2,

halogen,

OR^5 wherein R^5 is as defined above,

CN,

CO_2R^5 wherein R^5 is as defined above,

SO_3R^5 wherein R^5 is as defined above,

CHO, or

COR^5 wherein R^5 is as defined above;

R^2 and R^3 are the same or different and independently selected from hydrogen,

alkyl,

$-(CH_2)_v$-aryl wherein v is an integer from 1 to 5,

$-(CH_2)_v$-heteroaryl wherein v is as defined above,

$-(CH_2)_v$-cycloalkyl wherein v is as defined above,

$-(CH_2)_p$-X-$(CH_2)_q$-aryl wherein X is O or S and p and q is each zero or an integer of 1 to 5, and the sum of p + q is not greater than an integer of 5,

$-(CH_2)_p$-X-$(CH_2)_q$-heteroaryl wherein X, p, and q are as defined above,

$-(CH_2)_tNR^6R^{6a}$, wherein t is zero or an integer of from 1 to 9 and R^6 and R^{6a} are each the same or different and are as defined above for R^5,

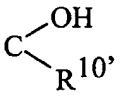
$-(CH_2)_vSR^5$, wherein v and R^5 are as defined above,

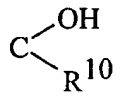
$-(CH_2)_vCO_2R^5$, wherein v and R^5 are as defined above, or

$-(CH_2)_vCONR^6R^{6a}$, wherein R^6 and R^{6a} are the same or different and are as defined above for R^5 and v is as defined above;

R^3 is additionally $-(CH_2)_rR^7$ wherein r is an integer from 1 to 5 and R^7 is 1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl, or 1,3,-dihydro-1,3-dioxo-benzo[f]isoindol-2-yl;

Y is CH or N;

Z is 

wherein R^{10} is as defined above for R^2 and R^3, and is independently the same or different from R^2 and R^3 provided that when Z is  , then R^4 must be OH,

C=O,

$C=NOR^5$ wherein R^5 is as defined above, or

$C=N-NR^6R^{6a}$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^5;

W is $-CHR^5$ wherein R^5 is as defined above;

n is zero or an integer of 1;

R^4 is OH,

NR^6R^{6a} wherein R^6 and R^{6a} are the same or different and are as defined above for R^5, when R^4 is NR^6R^{6a} then Z must be C=O or

$NHOR^9$ wherein R^9 is hydrogen, alkyl, or benzyl;

and corresponding isomers thereof; or a pharmaceutically acceptable salt thereof.

Preferred compounds to be employed include:

4-Oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

4-Oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid, potassium salt;

N-Hydroxy-4-oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyramide;

E/Z-4-Hydroxyimino-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

E/Z-4-Benzyloxyimino-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

4-Oxo-4-[4-(4-phenyl-piperazin-1-yl)-phenyl]-butyric acid;

(±)3-Methyl-5-oxo-5-[4-(4-phenyl-piperidin-1-yl)-phenyl]-pentanoic acid;

4-Oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

4-Oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid, potassium salt;

N-Hydroxy-4-oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyramide;

E/Z-4-Hydroxyimino-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

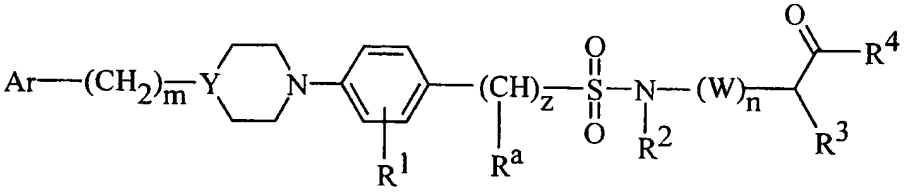
E/Z-4-Benzyloxyimino-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid;

4-Oxo-4-[4-(4-phenyl-piperazin-1-yl)-phenyl]-butyric acid; and

(±)3-Methyl-5-oxo-5-[4-(4-phenyl-piperidin-1-yl)-phenyl]-pentanoic acid.

A compound which is 4-oxo-4-[4-(4-phenyl-piperidin-1-yl)-phenyl]-butyric acid.

Similar compounds which are sulfonamide derivatives have the formula:



wherein:

Ar is selected from phenyl;

phenyl substituted with alkyl, -NO-$_2$, halogen, -OR^5, -CN, -CO$_2$R^5, -SO$_3$R^5, -CHO, -COR^5, -CONHR^5, -NHR^5, or -NHCOR^5;

heteroaryl; or

2-naphthyl;

R^1 is hydrogen, methyl, $-NO_2$, -Cl, $-NH_2$, $-NHCO_2CH_3$, -OH, or $-CO_2H$;

R^2 and R^3 are the same or different and are independently selected from hydrogen, alkyl, $-(CH_2)_v$-aryl, $-(CH_2)_v$-heteroaryl, $-(CH_2)_v$-cycloalkyl, $-(CH_2)_p$-X-$(CH_2)_q$-aryl, $-(CH_2)_p$-X-$(CH_2)_q$-heteroaryl, $-(CH_2)_tNR^6R^{6a}$, $-(CH_2)_vR^7$, $-(CH_2)_vCO_2R^5$, $-(CH_2)_vCONR^6R^{6a}$, or $-(CH_2)_vSR^5$;

m is zero or 1;

Y is CH or N; provided that when m = 1, Y does not = N;

z is zero or 1;

W is $-CHR^8$;

n is zero or 1;

R^4 is -OH, $-NR^6R^{6a}$, or $-NHOR^9$;

R^5 is hydrogen or alkyl;

v is 1 to 5;

X is O or S;

p and q are independently 1 to 5, provided that p + q is not greater than 5;

t is 1 to 9;

R^6 and R^{6a} are each the same or different and are hydrogen or alkyl;

R^7 is 1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl, or 1,3-dihydro-1,3-dioxo-benzo[f]isoindol-2-yl;

R^8 is hydrogen or alkyl; and

R^9 is hydrogen, alkyl, or benzyl; or

a pharmaceutically acceptable salt thereof.

Specific sulfonamide derivatives to be employed in the present method include:

[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-acetic acid;

N-Hydroxy-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-acetamide;

3-[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(±)-5-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

[4-(4-Phenyl-piperazin-1-yl)-benzene-sulfonylamino]-acetic acid;

{Isobutyl-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonyl]amino}-acetic acid;

(S)-4-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-butyric acid;

(R)-2-[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-3-tritylsulfanyl-propionic acid, sodium salt;

(R)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid, disodium salt, monohydrate;

(S)-2-{4-[-4-(4-Hydroxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(S)-2-{4-[-4-(4-Chloro-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid, hydrochloride;

(R)-3-Mercapto-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid, trifluoracetic acid salt;

(S)-2-[4-(4-Benzyl-piperidin-1-yl)-benzenesulfonylamino]-3-phenyl-propionic acid;

(S)-3-(4-Benzyloxy-phenyl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-(4-Hydroxy-phenyl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperazin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-2-{4-[-4-(3-Methoxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(S)-2-{4-[-4-(3-Hydroxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid hydrobromide;

(S)-2-{4-[-4-(4-Methoxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(R)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-acetic acid;

N-Hydroxy-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-acetamide;

3-[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(±)-5-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

[4-(4-Phenyl-piperazin-1-yl)-benzene-sulfonylamino]-acetic acid;

{Isobutyl-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonyl]amino}-acetic acid;

(S)-4-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-butyric acid;

(R)-2-[4-(4-Phenyl-piperidin-1-yl)-benzenesulfonylamino]-3-tritylsulfanyl-propionic acid, sodium salt;

(R)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid, disodium salt, monohydrate;

(S)-2-{4-[-4-(4-Hydroxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(S)-2-{4-[-4-(4-Chloro-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid, hydrochloride;

(R)-3-Mercapto-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid, trifluoracetic acid salt;

(S)-2-[4-(4-Benzyl-piperidin-1-yl)-benzenesulfonylamino]-3-phenyl-propionic acid;

(S)-3-(4-Benzyloxy-phenyl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-(4-Hydroxy-phenyl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperazin-1-yl)-benzenesulfonylamino]-propionic acid;

(S)-2-{4-[-4-(3-Methoxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(S)-2-{4-[-4-(3-Hydroxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid hydrobromide;

(S)-2-{4-[-4-(4-Methoxy-phenyl)-piperazin-1-yl]-benzenesulfonylamino}-3-phenyl-propionic acid;

(R)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-4-Methyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-pentanoic acid;

(S)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid;

(R)-3-Phenyl-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid; and

(S)-3-(1H-Indol-3-yl)-2-[4-(4-phenyl-piperidin-1-yl)-benzenesulfonylamino]-propionic acid.

Additional specific compounds which can be used include:

2-(Dibenzofuran-2-sulfonylamino)-3-(4-fluoro-phenyl)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-3-phenyl-propionic acid;

3-(4-tert-Butoxy-phenyl)-2-(dibenzofuran-2-sulfonylamino)-propionic acid;

(Dibenzofuran-2-sulfonylamino)-phenyl-acetic acid;

3-tert-Butoxy-2-(dibenzofuran-2-sulfonylamino)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-3-(1H-imidazol-4-yl)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-3-hydroxy-propionic acid;

3-Benzyloxy-2-(dibenzofuran-2-sulfonylamino)-propionic acid;

6-Benzyloxycarbonylamino-2-(dibenzofuran-2-sulfonylamino)-hexanoic acid;

5-Benzyloxycarbonylamino-2-(dibenzofuran-2-sulfonylamino)-pentanoic acid;

(Dibenzofuran-2-sulfonylamino)-(4-methoxy-phenyl)-acetic acid;

3-Chloro-2-(dibenzofuran-2-sulfonylamino)-propionic acid;

3-(4-Benzyloxy-phenyl)-2-(dibenzofuran-2-sulfonylamino)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-5-p-tolyl-sulfanylamino-pentanoic acid;

2-(Dibenzofuran-2-sulfonylamino)-4-mercapto-butyric acid;

3-(4-Bromo-phenyl)-2-(dibenzofuran-2-sulfonyl-amino)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-butyric acid;

1-(Dibenzofuran-2-sulfonylamino)-cyclopropane-carboxylic acid;

3-(4-Chloro-phenyl)-2-(dibenzofuran-2-sulfonyl-amino)-propionic acid;

2-(Dibenzofuran-2-sulfonylamino)-3-(1H-indol-3-yl)-propionic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(4-fluoro-benzenesulfonylamino)-hexanoic-acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(4-methoxy-benzenesulfonylamino)-hexanoic acid;

6-(4-Bromo-benzenesulfonylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic-acid;

6-(2-Acetylamino-thiazole-5-sulfonylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic-acid;

6-(4-Acetylamino-benzenesulfonylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic-acid;

6-Benzenesulfonylamino-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(pentane-1-sulfonylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(naphthalene-2-sulfonylamino)-hexanoic-acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(naphthalene-1-sulfonylamino)-hexanoic-acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-phenyl-ethenesulfonylamino)-hexanoic-acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-phenyl-acetylamino-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-chloro-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-chloro-phenoxy)-2-methyl-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(pyridin-4-ylsulfanyl)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(2,4-dichloro-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-thiophen-2-yl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(3-phenyl-acryloylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(7-phenyl-heptanoylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(2-trifluoromethyl-phenyl)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-phenoxy-butyrylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-phenyl-sulfanyl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-phenoxy-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(3,4-dimethoxy-phenyl)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-tert-butyl-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(3,4-dimethoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-cyclopent-1-enyl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-methoxy-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(naphthalen-1-yloxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-nitro-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[4-(4-chloro-3-methyl-phenoxy)-butyrylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(4-methoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-pyridin-3-yl-acetylamino)-hexanoic acid;

6-(2-Benzo[1,3]dioxol-5-yl-acetylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-pyridin-2-yl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-tert-butyl-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(3,4-dimethoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-cyclopent-1-enyl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-methoxy-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(naphthalen-1-yloxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-nitro-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[4-(4-chloro-3-methyl-phenoxy)-butyrylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(4-methoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-pyridin-3-yl-acetylamino)-hexanoic acid;

6-(2-Benzo[1,3]dioxol-5-yl-acetylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-pyridin-2-yl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[4-(4-nitro-phenyl)-butyrylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-tert-butyl-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(3,4-dimethoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-cyclopent-1-enyl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[2-(4-methoxy-phenoxy)-acetylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(4-phenyl-butyrylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[4-(4-chloro-3-methyl-phenoxy)-butyrylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(4-chloro-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(4-methoxy-phenyl)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-pyridin-3-yl-acetylamino)-hexanoic acid;

6-(2-Benzo[1,3]dioxol-5-yl-acetylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2-naphthalen-1-yl-acetylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-[3-(4-chloro-phenoxy)-propionylamino]-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(6-phenyl-hexanoylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(4-thiophen-2-yl-butyrylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(2,4,6-triisopropyl-benzoylamino)-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-isobutoxycarbonylamino-hexanoic acid;

2-(4′-Bromo-biphenyl-4-sulfonylamino)-6-(9H-fluoren-9-ylmethoxycarbonylamino)-hexanoic acid;

6-(Adamantan-1-yloxycarbonylamino)-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid; and

6-Allyloxycarbonylamino-2-(4′-bromo-biphenyl-4-sulfonylamino)-hexanoic acid.

Numerous succinamide MMP inhibitors are known and can be utilized in the method of this invention. Typical succinamides include:

2S,N^1-Dihydroxy-3R-isobutyl-N^4-{1S-[2-(2-methoxy-ethoxymethoxy)-ethylcarbamoyl]-2,2-dimethyl-propyl}-succinamide;

2S-Allyl-N^1-hydroxy-3R-isobutyl-N^4-{1S-[2-(2-methoxy-ethoxymethoxy)ethylcarbamoyl]-2-phenyl-ethyl}-succinamide;

2S-Allyl-N^1-hydroxy-3R-isobutyl-N^4-{1S-[2-(2-methoxy-ethoxymethoxy)ethylcarbamoyl]-2,2-dimethyl-propyl}-succinamide;

2S-Allyl-N^1-hydroxy-3R-isobutyl-N^4-(1S-{2-[2-(2-methoxy-ethoxy)-ethoxy]-ethylcarbamoyl]-2,2-dimethyl-propyl}-succinamide;

2S-Allyl-N^4-{1S-[2,2-di-(methoxymethyl)-propylcarbamoyl}-2,2-dimethyl-propyl]-N^1-hydroxy-3R-isobutyl-succinamide;

2S-Allyl-N^4-{1S-[2,2-di-(methoxymethyl)-butylcarbamoyl]-2,2-dimethyl-propyl}-N^1-hydroxy-3R-isobutyl-succinamide;

N^4-Hydroxy-2R-isobutyl-N^1-{1S-[2-(2-methoxy-ethoxy)-ethylcarbamoyl]-2,2-dimethyl-propyl}-3S-(thiophen-2-yl-sulfanylmethyl)-succinamide;

N^4-Hydroxy-2R-isobutyl-N^1-(1S-{2-[2-(2-methoxy-ethoxy)-ethoxy]-ethylcarbamoyl}-2,2-dimethyl-propyl)-3S-(thiophen-2-yl-sulfanylmethyl)-succinamide;

N^1-{1S-[2,2-Di-(methoxymethyl)-propylcarbamoyl]-2,2-dimethyl-propyl}-N^4-hydroxy-3R-isobutyl-3S-(thiophen-2-yl-sulfanylmethyl)-succinamide;

N^4-Hydroxy-2R-isobutyl-N^1-{1S-[2-(2-methoxy-ethoxy)-ethylcarbamoyl]-2,2-dimethyl-propyl}-3S-propyl-succinamide;

N^4-(1S-Cyclobutylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclopentylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclohexylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cycloheptylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2-mercapto-2-methyl-propyl)-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-(3-phenyl-propenyl)-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-2S,N^1-dihydroxy-3R-(3-phenyl-propyl)-succinamide;

N^4-[2,2-Dimethyl-1S-(2-phenyl-cyclopropylcarbamoyl)-propyl]-2S,N^1-dihydroxy-3R-isobutyl-succinamide;

2S-Allyl-N^4-(1-cyclopropylcarbamoyl-2,2-dimethyl-propyl)-N^1-hydroxy-3R-isobutyl-succinamide;

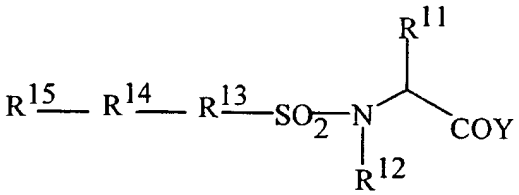
2S-Allyl-N^4-(1S-cyclopropylcarbamoyl-2-mercapto-2-methyl-propyl)-N^1-hydroxy-3R-isobutyl-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-N^1-hydroxy-3R-isobutyl-2S-(thiophen-2-ylsulfanylmethyl)-succinamide;

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-N^1-hydroxy-2S-(4-hydroxy-phenylsulfanylmethyl)-3R-isobutyl-succinamide; and

N^4-(1S-Cyclopropylcarbamoyl-2,2-dimethyl-propyl)-2S-(1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-N^1-hydroxy-3R-isobutyl-succinamide.

Another especially preferred group of MMP inhibitors to be utilized in the method of this invention are the sulfonated amino acid derivatives described in WO 97/27174, incorporated herein by reference. Those compounds have the general structure



where R^{11} is substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaryl, or substituted or unsubstituted heteroaryl alkyl;

R^{12} is hydrogen, or a group as defined for R^{11};

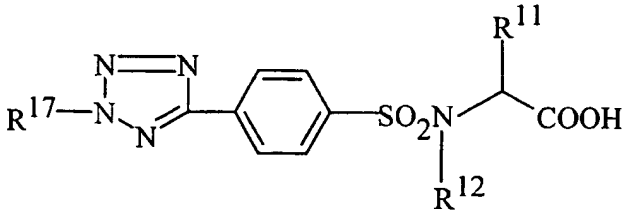
R^{13} is a single bond, substituted or unsubstituted arylene, or substituted or unsubstituted heteroarylene;

R^{14} is a single bond, $-(CH_2)_{1 \text{ or } 2}-$, -CH=CH-, -C≡C-, -CO-, -CONH-, -N=N-, NH, N-alkyl, -NHCONH-, -NHCO-, -O-, -S-, $-SO_2NH-$, $-SO_2NH-N=CH-$, or tetrazoldiyl;

R^{15} is substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, or substituted or unsubstituted non-aromatic heterocyclic group; and

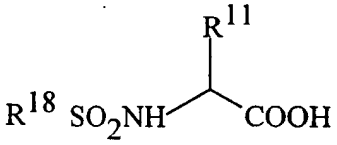
Y is NHOH or OH.

Especially preferred compounds to be employed in the method of this invention have the above formula wherein R^{13} is phenylene or substituted phenylene. Typical of such compounds that can be employed have the formula

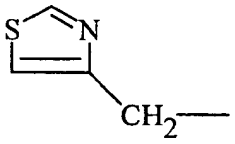
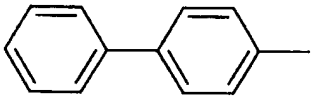
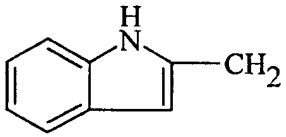
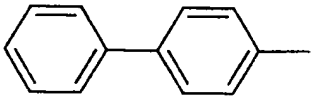
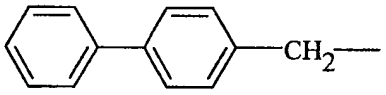
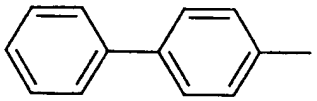
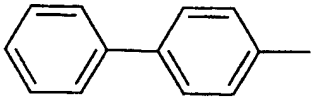
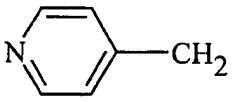
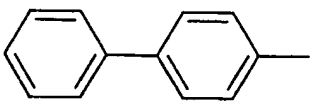


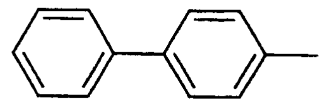
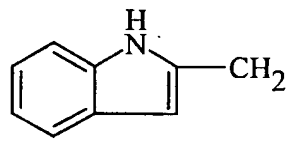
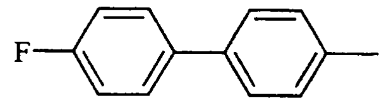
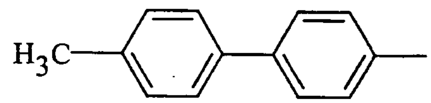
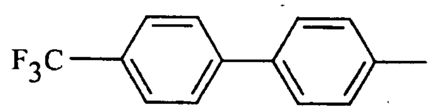
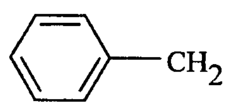
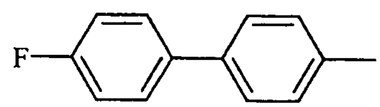
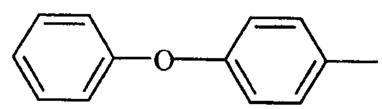
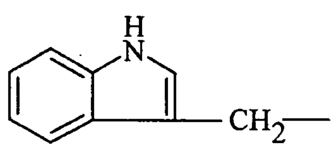
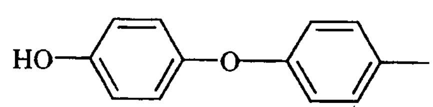
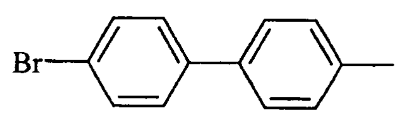
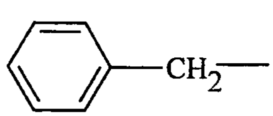
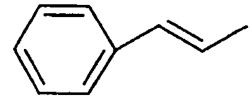
where R^{11} and R^{12} are as defined above, and R^{17} is substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl.

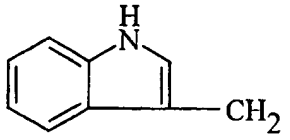
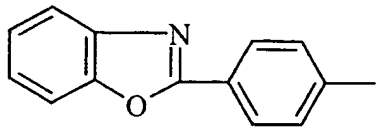
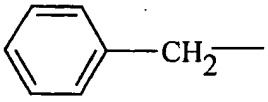
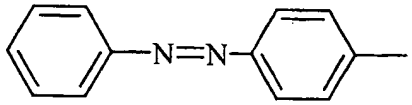
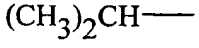
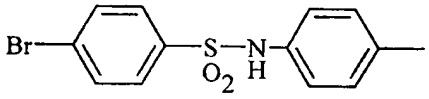
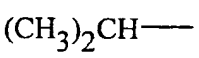
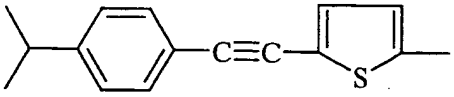
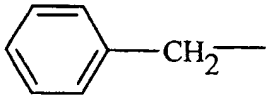
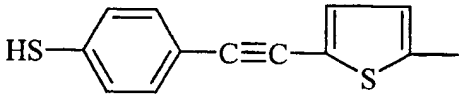
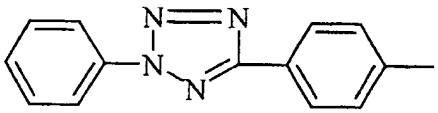
Especially preferred are compounds of the formula



wherein R^{11} and R^{18} are as follows:

R^{11}	R^{18}
	
	
	
CF_3CH_2—	
	

R^{11}	R^{18}
$HOOC-CH_2-$	
	
$(CH_3)_2CH-$	
$(CH_3)_2CH-$	
	
$(CH_3)_2CH-$	
	
$(CH_3)_2CH-$	
	

R^{11}	R^{18}
	
	
	
	
	
	

The following patents and applications covering MMP inhibitors are incorporated herein by reference: United States 5,753,653; WO 96/16027; WO 97/20824; WO 98/50348; WO 98/43963; WO 9832748; WO 98/17643; and EP 0780386. These include compounds such as shown below.

4-[2-(2-Carboxymethyl-4-phenyl-butylamino)-3-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butyrylamino)-3,3-methyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butyrylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-5-methyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butylamino)-2-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-valerylamino)-4-methyl-valerylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-phenyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino-benzoic acid methyl ester;

5-Methyl-3-(9-oxo-1,8-diaza-tricyclo[10.6.1.0,13,18]nonadeca-12(19),13,15,17-tetraen-10-ylcarbamoyl)-hexanoic acid;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-3,3-methyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-2-cyclohexylpropionylamino]-benzoic acid methyl ester benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-valerylamino)-4-methyl-valerylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butylamino)-3-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Methoxyaminocarbonylmethyl-4-phenyl-butylamino)-3-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-5-phenyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

5-Methyl-3-(9-oxo-1,8-diaza-tricyclo[10.6.1.0 13,18]nonadeca-12(19),13,15,17-tetraen-10-ylcarbamoyl)-1-hexylhydroxamic acid;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino]-benzoic acid methyl ester;

3-[2-(4-Methoxy-benzylsulfanyl)-2-methyl-1-phenylcarbamoyl-propylcarbamoyl]-5-methyl-hexanoic acid;

3-[2-(4-Methoxy-benzylsulfanyl)-2-methyl-1-phenylcarbamoyl-propylcarbamoyl]-5-methyl-hexanoic acid N-hydroxyamide;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-pentanoylamino)-2-cyclohexyl-acetylamino]-benzoic acid methyl ester;

2-(Phenyl-2-ethyl)benzoic acid N-hydroxy amide;

4-[2-(2-Acylhyrdazinomethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino]-benzoic acid methyl ester;

2-(Propylthio)-pyridine-3-N-(hydroxy)carboxamide;

4-[2-(2-Carboxymethyl-5-phenyl-pentanoylamino)-2-cyclohexylacetylamino]benzoic acid methyl ester;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-((thien-2-ylthio)methyl)succinyl]-L-phenylalanine-N-methylamide;

N-Hydroxy-5-phenylpentanamide;

4-[2-(2-Carboxymethyl-5-(3-hydroxyphenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-hydroxyphenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester, trifluoroacetate salt;

2-(Phenyl-2-ethyl)pyridine-3-N-hydroxycarboxamide;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)acetyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)acetyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-[3-(3-Hydroxy-phenyl)-propyl]-benzohydroxamic acid;

2-(Thiobenzyl)benzoic acid N-hydroxy amide;

1-(3-Phenyl-propyl)-pyrrolidine-2-hydroxamic acid;

4-[2-(2-Carboxymethyl-5-(5-hydroxyvaleroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(N'-methylureido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(triflouroacetamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-phenylacetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-2-phenylacetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-pentanoylamino)-2-cyclohexyl-acetylamino]-benzoic acid methyl ester;

2-[3-(3-Amino-phenyl)-propyl]-benzohydroxamic acid;

cis-4-Benzyloxy-pyrrolidine-2-carboxylic acid;

4-[2-(2-Carboxymethyl-5-(3-amino-4-(trifluoromethyl)phenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(methanesulfamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

N-Cbz-L-Tyrosine;

N-Boc-L-Tryptophan;

4-[2-(Carboxy-2-o-tolyl-propionylamino-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-[2-(Carboxymethyl-hepanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-n-butylphenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-n-butylphenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-(2-thienyl)acetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-(3-aminophenyl)-butyryl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(biphen-4-yl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

cis-4-Benzylsulfanyl-pyrrolidine-2-carboxylic acid;

2-Cyclohexylmethyl sulfonyl-benzoic acid;

Pyrrolidine-1-carbothioic acid phenethyl-amide;

3-(2-Methyl-thiazol-4-yl)-N-phenethyl-propionamide;

N-Phenyl-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-imidazol-4-yl]-propionamide;

3-(3H-Imidazol-4-yl)-N-phenethyl-propionamide;

4-[2-(2-Carboxymethyl-5-(formamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-Cyclohexylmethyl sulfonyl-benzohydroxamic acid;

[2-Oxo-3-(3-phenyl-propyl)-tetrahydro-furan-3-yl]-acetic acid;

4-[2-(2-Carboxymethyl-5-(fluoren-2-yl)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-(3-thienyl)acetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Benzylthio-3-carboxy-propionylamino)-4-methylpentanoylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-(2-indolyl)butyrylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

1-Allyl-3-(2-hydroxyethyl)-2-thiourea;

3-(1-Hydroxyimino-propyl)-6-phenyl-hexanoic acid;

2-(3H-Imidazol-4-ylmethyl)-N 1,N 4-diphenethyl-succinamide;

3-(2-Hydroxymethyl-3H-imidazol-4-yl)-N-phenethyl-propionamide;

6-Phenyl-3-propionyl-hexanoic acid;

4-{2-([2-Hydroxyamino-2-hydroxyimino-ethyl]-5-phenyl-pentanoylamino)-4-methyl-pentanoylamino}-benzoic acid methyl ester;

4-[2-(2-(2-Phenylcyclopropyl)succinylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid trifluoroacetate salt;

3-[1-(5,6-Dichloro-1H-benzoimidazol-2-yl)-3-methyl-butylcarbamoyl]-5-methyl-hexanoic acid;

6-Biphenyl-4-yl-3-[1-(5,6-dichloro-1H-benzoimidazol-2-yl)-3-methyl-butylcarbamoyl]-5-methyl-hexanoic acid;

2-Carboxymethyl-heptanoyl-2-(N-methylcarboxamide)piperidine;

4-[2-(2-(2-Phenylcyclopropyl)succinylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-Carboxymethyl-heptanoyl-3-(N-methylcarboxamide)-hexahydropyridazine;

6-Biphenyl-4-yl-3-[1-[3-(3-hydroxy-ethyl)-phenylcarbamoyl]-2,2-dimethyl-propylcarbamoyl]-hexanoic acid;

2R-(3-(4-Biphenyl)propyl-N-(2R-hydroxy-3-(2-hydroxyphenyl)-5-methyl-3S-hexyl)succinamide;

6-Biphenyl-4-yl-3-[1-[3-(2-aminoethyl)-phenylcarbamoyl]-2,2-dimethyl-propylcarbamoyl]-hexanoic acid;

2R-(3-(4-Biphenyl)propyl)-N-(diphenylmethyl)succinamide;

2R-(3-(4-Biphenyl)propyl)-N-(phenylmethyl)succinamide;

2-(2-Oxo-imidazolidin-4-ylmethyl)-5-phenyl-pentanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N1-[1-(5,6-dichloro-1H-benzoimidazol-2-yl)-3-methyl-butyl]-N4-hydroxy-succinamide hexanoic acid;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid, N-hydroxyamide;

2R-(3-(4-Biphenyl)propyl)-N-((1-hydroxy-1-methylethyl)phenylmethyl)-succinamide;

6-Biphenyl-4-yl-3-[1-phenylcarbamoyl-2-(4-cyano-benzylsulfanyl)-2-methyl-propylcarbamoyl]-hexanoic acid;

4-{2-[2-Carboxymethyl-5-(4'-hydroxy-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

1-(N-Methyl-N-phenethylthiocarbomyl)-pyrrolidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-({cyclohexyl-[2-(4-sulfanoyl-phenyl)-ethylcarbamoyl]-methyl}-carbamoyl)-hexanoic acid;

3R(6-(4-Biphenyl)-3-(N-benzylcarbamoyl))-hexanoic acid N-hydroxyamide;

[3-(3-Biphenyl-4-yl-propyl)-2-oxo-pyrrolidin-3-yl]-acetic acid;

2-Benzylsulfonyl-cyclopent-1-ene-carboxylic acid hydroxamide;

[2-Oxo-3-(3-phenyl-propyl)-pyrrolidin-3-yl]-acetic acid;

[3-(3-Naphthalen-2-yl-propyl)-2-oxo-pyrrolidin-3-yl]-acetic acid;

2-Benzylsulfonyl-cyclohex-1-enecarboxylic acid hydroxy amide;

6-Benzylsulfonyl-cyclohex-1-enecarboxylic acid hydroxy amide;

2R-(3-(4-Biphenyl)propyl)-N-(3-methylpyridine)succinamide;

{3-[3-(3-Hydroxy-phenyl)-propyl]-2-oxo-pyrrolidin-3-yl}-acetic acid;

6-Biphenyl-4-yl-{[cyclohexyl-(3-morpholin-4-yl-propylcarbamoyl)-methyl]-carbamoyl}hexanoic acid;

[2-Oxo-3-(3-biphenyl-propyl)-tetrahydro-furan-3-yl]-acetic acid;

4-[2-(2-Thioamidomethyl-5-phenyl-valerylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

4-[2-(2-Amino-2-hydroxyimino-ethyl-5-phenyl-valerylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfamoyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(2-hydroxyethylsulfamoyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

1-(N-Hydroxy)-3-(2-bibenzyl)urea;

4-(2-{5-[7-(2-Amino-acetylamino)-9H-fluoren-2-yl]-2-carboxymethyl-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester TFA salt;

3R-(6-(4-Biphenyl)propyl)-N-(3-methylpyridinecarbamoyl)-hexanoic acid N-hydroxy amide;

6-Biphenyl-4-yl-3-[cyclohexyl-(4-(2-hydroxy-ethylsulfamoyl)-phenylcarbamoyl)-methylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[cyclohexyl-(4-(2-dimethylamino-ethylsulfamoyl)-phenylcarbamoyl)-methylcarbamoyl]-hexanoic acid, trifluoroacetate salt;

4-(2-{2-Carboxymethyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-(2-hydroxy-ethyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-(2-{[5-Hydroxyamino-3-(3-phenyl-propyl)-3,4-dihydro-2-H-pyrrole-3-carbonyl]-amino}-4-methyl-pentanoylamino)benzoic acid methyl ester;

5-Hydroxyamino-3-(3-phenyl-propyl)-3,4-dihydro-2-H-pyrrole-3-carboxylic acid(2-cyclohexyl-1-methylcarbamoyl-ethyl)amide;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-(3-morpholin-4-yl-sulfamoyl)-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfanyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfonyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(5-Biphenyl-4-yl-2-carboxymethyl-pentanoylamino)-pent-4-enoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-(2-{[5-Hydroxyamino-3-(3-pentyl)-3,4-dihydro-2-H-pyrrole-3-carbonyl]-amino}-4-methyl-pentanoylamino)benzoic acid methyl ester;

5-Hydroxyamino-3-(3-pentyl)-3,4-dihydro-2-H-pyrrole-3-carboxylic acid(2-cyclohexyl-1-methylcarbamoyl-ethyl)amide;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-cyano-biphenyl-4-yl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-y-3-(R)-(2-hydroxy-1-(S)-phenyl-ethylcarbamoyl)-hexanoic acid;

3-(R)-(1-(R)-Benzyl-2-hydroxy-ethylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-hydroxymethyl-ethylcarbomyl)-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-pyridin-4-yl-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]benzoic acid methyl ester;

6-Biphenyl-4-yl(2-hydroxy-2-methyl-1-phenylcarbamoyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl(2-hydroxy-2-methyl-1-phenylcarbamoyl-propylcarbamoyl)-hexanoic acid;

3-{2-Allylsufamyl-2-methyl-1-[2-(4-sulfamoyl-phenyl)-ethylcarbamoyl]-propylcarbamoyl}-6-biphenyl-4-yl-hexanoic acid;

4-[2-(5-Biphenyl-4yl-2-carboxymethyl-pentanoylamino)-4,5-dihydroxy-pentanoylamino]-benzoic acid methyl ester;

4-(2-{5-[4′-(2-Amino-ethoxy)-biphenyl-4-yl]-2-carboxymethyl-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester;

6-Biphenyl-4-y-3-(R)-(2-hydroxy-1-(S)-phenyl-ethylcarbamoyl)-hexanehydroxamic acid;

3-(R)-(1-(R)-Benzyl-2-hydroxy-ethylcarbamoyl)-6-biphenyl-4-yl-hexanehydroxamic acid;

N-[5-(Biphenyl-4-yl)-2-(N-hydroxyformamido)methylpentanoyl]-tert-leucine, N-(pyrid-4-yl)amide;

[3-(3-Naphthalen-2-yl-propyl)-2-oxo-tetrahydro-furan-3-yl]-acetic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-hydroxymethyl-ethylcarbomyl)-hexanehydroxamic acid;

4-[2-(2-Carboxymethyl-5-naphthalen-2-yl-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

3-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-5-methyl-hexanoicacid;

N1-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propyl]-N4-hydroxy-2-isobutyl-succinamide;

4-{2-[2-Carboxymethyl-5-(2-fluoro-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

6-Biphenyl-4-yl-3(R)-(1(S)-hyroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic acid;

4-{2-[5-Biphen-4-yl-2-(1-carboxy-ethylamino)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

6-Biphenyl-4-yl-3(R)-(1(S)-hyroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanehydroxamic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

2-(Biphenyl-4-ylsulfonyl)-cyclohex-1-enecarboxylic acid hydroxyamide;

6-(Biphenyl-4-ylsulfonyl)-cyclohex-1-enecarboxylic acid hydroxyamide;

2-Phenethylsulfanyl-cyclohex-1-enecarboxylic acid hydroxyamide;

6-(4′-cyano-biphenyl-4-yl)-3-[2-hydroxy-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylcarbamoyl}-pyrrolidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4S-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-(2-hydroxy-3,3,3-trifluoropropyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

2-Benzylsulfanyl-cyclohexancarboxylic acid hydroxamide;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylcarbamoyl}-pyrrolidine-2-carboxylic acid;

trans-2-Benzylsulfanyl-cyclohexancarboxylic acid hydroxamide;

4-[2-(2-Carboxymethyl-5-(4-(2-methylthiazol-4-yl)phenyl)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylthiocarbamoyl}-pyrrolidine-2-carboxylic acid;

3-[(Cyclohexyl-(4-(2-hydroxy-ethylsulfamoyl)-phenylcarbamoyl)-methyl)-carbamoyl]-6-(4-pyridin-4-yl-phenyl)-hexanoic acid trifluoroacetate salt;

trans-2-(Biphenyl-4-yl-methylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2,2-dimethyl-but-3-enylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2,2-dimethyl-but-3-enylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanoic acid;

3-(R)-(2-(R)-Benzyloxy-1-(S)-hydroxymethyl-propylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

4-[4-Methyl-2-(2-nitromethyl-5-phenyl-pentanoylamino)-pentanoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[3-methyl-1-(4-(2-hydroxyethylsulfamoyl)-phenylcarbamoyl)-butylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2-phenyl-ethylcarbamoyl)-hexanoic acid;

N1-(1-Benzyl-2-hydroxy-ethyl)-2-(3-biphenyl-4-yl-propyl)-N4-hydroxy-succinamide;

6-Biphenyl-4-yl-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanehydroxamic acid;

N-Hydroxy-2-[2-Oxo-3-(3-phenyl-propyl)-tetrahydro-furan-3-yl]-acetamide;

4-[2-(2-Carboxymethyl-5-(2-hydroxy-biphen-4-yl)-valeroylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

N1-(2-Benzyloxy-1-hydroxymethyl-propyl)-2-(3-biphenyl-4-yl-propyl)-N^4-hydroxy-succinamide;

trans-2-(4-Phenoxy-benzylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

2-(4-Indol-1-yl-benzylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

6-Biphenyl-4-yl-3-[2-hydroxy-2-methyl-1-(4S-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-ylcarbamoyl)-hexanoic acid;

5-Biphenyl-4-yl-2-[(formyl-hydroxy-amino)-methyl]-pentanoic acid{1-[4-(2-dimethylamino-ethylsulfamoyl)-phenylcarbamoyl]-3-methyl-butyl}-amide;

2-(3-Biphenyl-4-yl-propyl)-N4-hydroxy-N1-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-yl)-succinamide;

6-Biphenyl-4-yl-3-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-ylcarbamoyl)-hexanoic acid;

N-[2,2-Dimethyl-1S-(pyridin-4-ylcarbamoyl)-propyl]-3R-thiophen-3-yl-succinamic acid;

4-[2S-(2R-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxy-propionylamido)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

3-(R)-(2-Benzyloxy-phenyl)-1-(S)-hydroxymethyl-ethylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-(S)-(4-hydroxy-benzyl)-ethylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxyimino-ethyl)-hexanoic acid;

N-[2-(3-(4-biphenyl)propyl)-5,5-difluoro-4-oxopentanoyl)-L-t-leucine, N'-4-(methylthio)phenyl amide;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-(S)-(4-hydroxy-benzyl)-ethylcarbamoyl)-hexanehydroxamic acid;

4-{2-[2-carboxymethyl-5-(4'-sulfamoyl-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

2-(2-Biphenyl-4-yl-ethylsulfanyl)-cyclohexane carboxylic acid hydroxyamide;

3-Acetyl-6-biphenyl-4-yl-3-hexanoic acid;

N-[5-(Biphen-4-yl)-2-(1-carboxy-2-hydroxybut-1-yl)pentanoyl]-t-L-leucine, N'-(4-methylthiophenyl)amide;

6-Biphenyl-4-yl-3-(2-hydroxy-cyclohexylcarbamoyl)-hexanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N^4-hydroxy-N1-(2-hydroxy-cyclohexyl)-succinamide;

6-Biphenyl-4-yl-3-(1-hydroxyimino-ethyl)-hexanoic acid hydroxamide;

6-Biphenyl-4-yl-3-(2-Hydroxy-cyclohexylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid ethyl ester;

2-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxy-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

N-[5-(Biphen-4-yl)-2-(1-carboxy-2-hydroxyethyl)pentanoyl]-L-t-leucine, N'-(4-methylthiophenyl)amide;

3-(R)-(2-Hydroxy-1-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-6-(4-(2-methyl-thiazol-4-yl)-phenyl)-hexanoic acid;

3-(R)-(2-Hydroxy-1-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-6-(4-(2-methyl-thiazol-4-yl)-phenyl)-hexanehydroxamic acid;

5-Biphenyl-4-yl-2-(1-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-pentanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N-hydroxy-N′-(1-hydroxymethyl-3-methylsulfanyl-propyl)malonamide;

6-Biphenyl-4-yl-3-(3-hydroxy-piperidine-1-carbonyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(3-hydroxy-piperidine-1-carbonyl)-hexanoic acidhydroxyamide;

1-(4-Methoxy-benzenesulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1-[4-Bromo-phenoxy)-benzenesulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

N-(1-Benzyl-2-methoxy-ethyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamic acid;

N-(1-Benzyl-2-methoxy-ethyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamic hydroxamic acid;

6-Biphenyl-4-yl-3(R)-2(S)-hydroxy-(1(S)-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic acid;

3-(1-Benzyl-2-hydroxy-ethylcarbamoyl)-5-methyl-hexanoic acid;

N^1-(1-benzyl-2-hydroxy-ethyl)-N^4-hydroxy-2-isobutyl-succinamide;

6-Biphenyl-4-yl-3(R)-2(S)-hydroxy-(1(S)-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic hydroxamic acid;

1-[4-Bromo-phenoxy)-benzenesulfonyl)-piperidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-(2-hydroxy-1-hydroxmethyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-cyclohexyl-1-(S)-carbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(2-hydroxy-1-hydroxmethyl-propylcarbamoyl)-hexanoichydroxamic acid;

2S-[(1S-Benzyl-2-hydroxyethylcarbamoyl)-3R-biphenyl-4-yl-pyrrol-1-yl-methyl]-pentanoic acid;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-(2R-hydroxy-cyclohexyl-1R-yl)-succinamic acid;

2-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxamate-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

trans-2-(3-Biphenyl-4-yl-propyl)-cyclohexane carboxylic acid;

trans-2-(3-Biphenyl-4-yl-propyl)-cyclohexane carboxylic acidhydroxyamide;

6-Biphenyl-4-yl-3-(R)-(1-(S)-hydroxymethyl-2-(3-pyridyl)-ethylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-2-(S)-hydroxy-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanoic acid;

1-[4-Biphenyl-4-yloxy)-benzenesulfonyl)-piperidine-2-carboxylic acid;

1-[4-Biphenyl-4-yloxy)-benzenesulfonyl)-piperidine-2-carboxylic acidhydroxamide;

1-(4-Phenoxy-benzenesulfonyl)-piperidine-2-carboxylic acidhydroxamide;

6-Biphenyl-4-yl-2S-hydroxy-3R-(1S-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(1-(S)-hydroxymethyl-2-(3-pyridyl)-ethylcarbamoyl)-hexanehydroxamic acid;

6-Biphenyl-4-yl-2S-hydroxy-3R-(1S-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-hexanoic hydroxamic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-4-(tert-butoxycarbonyl)-piperazine-2-carboxylic acidhydroxyamide;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-piperazine-2-carboxylic acidhydroxyamide;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[2-hydroxy-1S-(1H-imidazol-4-yl-methyl)-ethyl]-succinamic acid trifluoroacetate;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[1S-(methoxy-methylcarbamoyl)-3-methyl-butyl]-succinamic acid;

N-(1-Acetyl-3-methyl-butyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-1-tetrahydrofuran-3-(S)-ylcarbamoyl)-hexanoic acid;

3-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-2-hydroxy-5-methyl-hexanoic acid-hydrochloride salt;

N^4-(2,2-Dimethyl-1-methylcarbamoyl-propyl)-2,N^1-dihydroxy-3-isobutyl-succinamide;

6-Biphenyl-4-yl-3-(R)-(2-oxo-azepan-3-(S)-ylcarbamoyl)-hexanoic acid;

N-(1-Benzyl-2-hydroxy-ethyl)-3-(4-biphenyl-4-yl-pyrazol-1-yl)-succinamic acid;

N-(8-Oxo-4-oxa-1,7-diaza-tricyclo[9.6.1.0 12,17]octadeca-11(18),12(17),13,15-tetraen-9R-yl)-3S-(3-phenyl-pyrrol-1-yl)-succinamic acid;

4-Acetyl-1-[4-phenoxy-benzenesulfonyl]-piperazine-2-carboxylic acid, N-hydroxyamide;

1-(Diphenylphosphinic)-piperidine-2-carboxylic acid hydroxamide;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[3S-(2RS-hydroxy-5-methyl)-hexyl]-succinamic acid;

N-(1-(S)-Benzyl-2-hydroxy-ethyl)-3-(R)-(2-biphenyl-4-yl-cyclopropylmethyl)-succinamic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-1-tetrahydrofuran-3-(S)-ylcarbamoyl)-hexanehydroxamic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-4-methyl-piperazine-2-carboxylic acid N-hydroxyamide;

4-(4-Methoxy-benzenesulfonyl)-thiomorpholine-3-carboxylic acidhydroxyamide;

3-(Diphenylphosphinic)-propanoic acid;

3-(Diphenylphosphinic)-propanoic acid hydroxyamide;

4-[2-(2-Carboxymethyl-5-(4-(3-hydroxy-propyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

1-[4-(4-Chlorophenoxy)benzenesulfonyl]-N-hydroxy-4-(N-methylcarbamoyl)piperazine-2-carboxamide;

4-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid N-hydroxyamide;

3-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

1-[4-Phenoxy-benzenesulfonyl]-piperazine-2-carboxylic acid, N-hydroxyamide;

4[4-Phenoxy-benzenesulfonyl]-thiomorpholine-3-carboxylic acid N-hydroxyamide;

3-[2-Biphenyl-4-yl-ethylsulfanyl]-tetrahydro-pyran--4-carboxylic acid N-hydroxyamide;

6-Biphenyl-4-yl-3-(carboxylic acid)-hexanoic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]piperdine-2-amidoxime;

2-(3-Biphenylnitrile-4-yl-pyrrol-1-yl)-3-carboxy-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

{3-[3-(3-Amino-phenyl)-propyl]-2-oxo-tetrahydro-furan-3-yl}-acetic acid;

6-Biphenyl-4-yl-2S-hydroxy-3R-(carboxylic acid)-hexanoic acid;

5-Biphenylvaleric acid;

1-[4-(Methoxy)-benzenesulfonyl]piperdine-2-amidoxime;

1-[4-Phenoxy-benzenesulfonyl]-4-methyl-piperazine-2-carboxylic acid N-hydroxyamide;

{3-(3-(3-Methylamino-phenyl)-propyl)-2-oxo-tetrahydro-furan-3-yl}-acetic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-azepan-3-(S)-ylcarbamoyl)-hexanehydroxamic acid;

4-(1H-Indole-2-sulfonyl)-thiomorpholine-3-carboxylic acid hydroxyamide;

1R-[4-Bromo-phenoxy)-benzenesulfonyl)-N-amino-piperidine-2-carboxamide;

2-(3-Biphenyl-4-yl-propyl)-3, N-4-dihydroxy-N^1-(1(S)-hydroxymethyl-3-methanesulfinyl-propyl)-succinamide;

N-(1-Benzyl-2-hydroxy-ethyl)-3-[3-(4′-carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-succinamic acid;

1-(Methyl-phenylphosphinic)-piperidine-2-(R)-carboxylic acid hydroxamide;

4-(4-(4-Chlorophenoxy)benzenesulfonyl)-N-hydroxy-morpholine-3R-carboxamide;

2S-[1R-(3-(4′-Cyano-biphenyl-4-yl)-pyrrol-1-yl)-N-(2,2-dimethyl-1S-hydroxymethylpropylcarbamoyl)-methyl)]-pentanoic acid;

2(S,R)-{1S-Benzyl-2-hydroxyethylcarbamoyl-[3R-(4′-cyano-biphenyl-4-yl)-pyrrol-1-yl]-methyl}pentanoic acid;

2S-[3-(Biphenyl-4-yl)-pyrrol-1R-yl-(1S-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-methyl]-5-hydroxypentanoic acid;

1-(1,3-Dihydro-isoindole-2-sulfonyl)-piperidine-2-carboxylic acid hydroxamide;

3-[3-(4′-Carbamoyl-biphenyl-4-yl]-pyrrol-1-yl)-N-(1-hydroxymethyl-2,2-dimethyl-propyl)-succinamic acid;

4-Methyl-1-(4-(4-chlorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochloride;

1-[4-Chlorophenoxybenzenesulfonyl]-N-hydroxy-2R-piperazinecarboxamide;

2-(3-Phenyl-propylsulfonyl)-cyclohexane carboxylic acid hydroxamide;

1-(Pyrolidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1-(Piperidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

4-[4-Bromo-phenoxy-benzenesulfonyl]-oxothiomorpholine-3-carboxylic acid-N-hydroxyamide;

1-[4-(4-Methoxy-phenylsulfanyl)-benzenesulfonyl]-piperdine-2-carboxylic acid hydroxyamide;

1-[4-(4-Nitrile-phenoxy)-benzenesulfonyl]-4-(tert-butoxycarbonyl)-piperazine-2-carboxylic acid N-hydroxyamide;

2S-[3-(Biphenyl-4-yl)-pyrrol-1R-yl-(1S-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-methyl]-pent-4-enoic acid;

6-Oxo-3-(4-phenoxy-benzenesulfonyl)-hexahydro-pyrimidine-4-carboxylic acid hydroxamate;

4-(t-Butoxycabonyl)-1-(4-(pyridin-2-yl)oxybenzensulfonyl)-N-hydroxy-piperazine-2-carboxamide;

4-[(4-Fluorophenoxy)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid-N-hydroxyamide;

4-[4-(Fluoro-phenoxy)-benzenesulfonyl]-oxothiomorpholine-3-carboxylic acid-N-hydroxyamide;

N-(2,2-Dimethyl-1S-hydroxymethyl-propyl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(1S-Benzyl-2-hydroxy-ethyl)-3S-(5-biphenyl-4-yl-furan-2-yl)-succinamic acid;

4-(4-Butoxy-benzenesulfonyl)-thiomorpholine-3-carboxylic acid hydroxyamide;

4-(4-Butoxy-benzenesulfonyl)-1-oxothiomorpholine-3-carboxylic acid hydroxyamide;

1-[4-(4-Fluorophenyl)benzenesulfonyl]-4-(tert-butoxycarboxyl)-2R-piperazine-2-carboxylic acid hydroxyamide;

1-((4-(4-Chlorophenyl)-piperazine)-1-sulfonyl)-piperidine-2-carboxylic acid hydroxamide;

cis-2-Phenethylsulfanyl-cyclohexanecarboxylic acid hydroxyamide;

N-(2-Hydroxy-1S-phenyl-ethyl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

1-[4-(4-Fluorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochoride;

1-(Diphenylphosphinic)-pyrolidine-2-(R)-carboxylic acid-hydroxyamide;

N,N-{(Diphenylphosphinic)-(acetic acid-sodium salt)}-hydrazide;

N-(1-Benzyl-2-hydroxy-ethyl)-3-(1-biphenyl-4-yl-1H-pyrrol-3-yl)-succinamic acid;

trans-2-Phenethylsulfonyl-cyclohexanecarboxylic acid hydroxyamide;

1-[4-(4-Fluorophenyl)-piperazine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

1-[4-(4-Fluorophenylsulfanyl)-benzenesulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

4-[4-(Bromo-phenoxy)-benzenesulfonyl]-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-(3-phenyl-pyrrol-1-yl)-succinamic acid;

3R-(3-Biphenyl-4-yl)-N-(2-hydroxy-1S-hydroxymethyl-2-methyl-propyl)-succinamic acid;

1-(Pyrrolidine-1-carbonyl)-pyrrolidine-2(R)-carboxylic acid;

1-(Pyrrolidine-1-carbonyl)-pyrrolidine-2(R)-carboxylic acid hyroxyamide;

1-Phenethylcarbamoyl-pyrrolidine-2(R)-carboxylic acid;

R-4-[4-(Bromophenoxy)-benzenesulfonyl]-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

4-(Ethoxycarbonyl)methyl-1-(4-(4-chlorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochloride;

N-(2R-Hydroxy-indan-1R-yl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(4,4-Dimethyl-2-oxo-tetrahydro-furan-3S-yl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-[3-(4-pyridin-4-yl-phenyl-4-yl)-pyrrol-1-yl]-succinamic acid;

1-Phenethylcarbamoyl-pyrrolidine-2-(R)-carboxylic acid hydroxyamide;

N-(2,2-Dimethyl-1S-methyl carbamoyl-propyl)-3R-[3-(4-propyl-phenyl)-pyrrol-1-yl]-succinamic acid;

1-(4-Benzyl-piperazine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

3(S)-N-hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

2(R)-4-Methyl-1-(4-(4-fluorophenyl)benzenesulfonyl)-N-hydroxy-piperazine-2-carboxamide;

N-(2,2-Dimethyl-1-methylcarbamoyl-propyl)-3-(5-biphenyl-4-yl-furan-2-yl)-succinamic acid;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-(3-pyridin-4-yl-pyrrol-1-yl)-succinamic acid;

1-((2-Pyridyl)-4-piperazine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

1-[4-(Pyridin-4-ylsulfamyl)-benzenesulfonyl]-piperdine-2-carboxylic acid hydroxyamide;

N-(4-Phenoxy-benzenesulfonyl)-D-tert-leucine;

N-(4-Phenoxy-benzenesulfonyl)-D-tert-leucine, N-hydroxyamide;

N-(8-oxo-4-oxa-1,7-tricyclo[9.6.1.0 12,17]octadeca-11(18),12(17),13,15-tetraen-9-yl)-3-[4-(4-pyridyl)-3-phenyl-pyrrol-1-yl)-succinamic acid;

3-[3-(4-Pyridyl)phenyl-4-yl-pyrrol-1-yl]-N-[2,2-dimethyl-1-(4-pyridyl)carbamoyl-propyl]-succinamic acid;

2,2-Dimethyl-4-[4-(pyridin-2-yloxy)-benzenesulfonyl]-thio-morpholine-3-carboxylic acid hydroxyamide;

N-[4-(4-Fluorophenoxyl)benzenesulfonyl)-D-tert-leucine;

N-[4-(4-Fluorophenoxyl)benzenesulfonyl)-D-tert-leucine, N-hydroxyamide;

2-[2-(N′-Acetyl-hydrazino)-2-oxo-ethyl]-5-biphenyl-4-yl-pentanoic acid;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide hydrochloride;

2-[4-(4-Chloro-phenoxy)-benzenesulfonylamino]-3,3-dimethyl-butyric acid;

2-[4-(4-Chloro-phenoxy)-benzenesulfonylamino)-N-hydroxy-3,3-dimethyl-butyramide;

3(R)-N-Hydroxy-4-(4-(fur-3-yl)phenoxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine, N-hydroxyamide;

2-[4-(Pyridin-2-yl-oxy)-benzenesulfonylamino]-3,3-dimethyl butyric acid;

2-[4-(Pyridin-2-yl-oxy)-benzenesulfonylamino]-N-hydroxy-3,3-dimethyl butyramide;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine;

3-[3-(4′-Carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

3-[3-(4′-Cyano-biphenyl-4-yl)-pyrrol-1-y]-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

2-(2-Biphenyl-4-yl-ethylsulfonyl)-cyclohex-1-ene-carboxylic acid hydroxyamide;

6-(2-Biphenyl-4-yl-ethyl sufonyl)-cyclohex-1-ene-carboxylic acid hydroxyamide;

N-(4-Pyridin-4-yl-oxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine;

3-[3-4′-Carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-N-[2,2-dimethyl-1-(pyridin-4-yl-carbamoyl)-propyl]-succinamic acid;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine, N-hydroxyamide;

1-(4-Phenoxy-piperdine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

3(R)-4-[4-(4-Bromo)phenoxybenzenesulfonyl]-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxylic acid;

N-(4-[4-Chloro-phenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine;

N-(4-[4-Chlorophenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine, N-hydroxyamide;

N-(4-[4-Chlorophenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylsulfoxy)-D-cysteine, N-hydroxyamide;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-2-ylsulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-3-ylsulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-4-ylsulfanyl)-butyric acid;

cis-2-(2-Phenyl-ethanesulfonyl)-cycloheaxanecarboxylic acid hydroxyamide;

3(R)-N-Hydroxy-4-(4-(imidaz-1-yl)phenoxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

4-[2-(2-Hydroxycabamoylmethyl-5-phenyl-pentanoylamino)-4-methyl-pentanoyl-benzoic acid methyl ester;

trans-2-(2-Phenyl-ethanesulfonyl)-cyclohexanecarboxylic acid hydroxyamide;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfanylmethyl)-butyric acid;

2-[4-(4-Chlorophenyl)-piperazine-1-sulfonylamino]-3-methyl-3-(pyridin-2-ylmethylsulfanyl)-butyric acid;

3R-[3-(4′-Cyano-biphenyl-4-yl)pyrrol-1-yl]-N-[2,2-dimethyl-1S-(pyridin-4-ylcarbamoyl)-propyl]-succinamic acid;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfanylmethyl)-butyric acid, N-hydroxyamide;

N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-3-[1-(4-fluorophenyl)-1H-pyrrol-3-yl]-succinamic acid;

2(R)-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-ylsulfanyl)-butyric acid;

2-(2-Biphenyl-4-yl-ethanesulfonyl)-cyclohexanecarboxylic acid hydroxamate;

2-[4-(4-Chlorophenyl)-piperazine-1-sulfonylamino]-3-methyl-3-(pyridin-2-ylmethylsulfanyl)-butyric acid, N-hydroxyamide;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfonylmethyl)-butyric acid;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfonylmethyl)-butyric acid, N-hydroxyamide;

3-tert-Butoxycarbonylmethylsulfanyl-2-(4-(4-fluoro-phenoxy)benzenesulfonylamino)-3-methyl-butyric acid;

1-(4-Phenylsulfanyl-piperidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1-[4-(4-Fluoro-phenoxy)-benzenesulfonyl]-3,3-dimethyl-5-oxo-piperazine-2-carboxylic acid;

N-(4-[4-Fluorophenoxy]-benzenesulfonylamino)-3-methyl-3-(1-benzyl-imidazole-2-yl-sulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-yl-sulfanyl)-butyric acid, hydroxyamide;

3(R)-N-Hydroxy-4-(4-((pyridin-4-yl)methyl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

1-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-4-(1-methyl-1H-imidazole-4-sulfonyl)-piperazine-2-carboxylic acid hydroxamide;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-[1-(4'-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

3-Carboxymethylsulfanyl-2-(4-(4-fluoro-phenoxy)-benzenesulfonylamino)-3-methyl-butyric acid;

2,2-Dimethyl-1-oxo-4-[4-(pyridin-4yloxy)-benzenesulfonyl]-1S14-thiomorpholine-3-carboxylic acid hydroamide;

1-[4-(Pyridin-2-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-(fur-3-yl)-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfanyl)-butyric acid;

2,2-Dimethyl-1-oxo-4-[4-(pyridin-4yloxy)-benzenesulfonyl]-1S14-thiomorpholine-3-carboxylic acid hydroamide;

{2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-2-hydroxycarbamoyl-1,1-dimethyl-ethylsulfanyl}-acetic acid tert-butyl ester;

1-[4-(Pyridin-4-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-Bromo-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfanyl)-butyric acid, hydroxyamide;

trans-2-(2-Biphenyl-4-yl-ethylsulfanyl)-cyclohexanecarboxylic acid hydroxyamide;

N-[1S-(1H-Imidazol-2-yl)-3-methyl-butyl]-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid formate;

N-Methyl-3-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N(4)-(2,2-Dimethyl-1S-hydroxymethyl-propyl)-N(1)-hydroxy-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succindiamide;

{2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-2-hydroxycarbamoyl-1,1-dimethyl-ethylsulfanyl}-acetic acid;

1-[4[(4-Fluoro-phenoxy)-benzenesulfonyl)]-3,3-dimethyl -5-oxo-piperazine-2-carboxylic acid hydroxyamide;

N-(4-[4-Bromophenoxy]-benzenesulfonylamino)-3-methyl-3-(1-benzyl-imidazole-2-yl-sulfanyl)-butyric acid;

3R-[3-(4′-Cyanobiphenyl-4-yl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-hydroxymethyl-propyl)-succinamic acid;

2-(R)-[4-(4-Iodophenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-yl-sulfanyl)-butyric acid;

□

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-hydroxymethyl-propyl)-succinamic acid;

2(R)-[4-(4-Iodo-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid, hydroxyamide;

2(R)-[4-(4-Nitrile-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid;

2-[4-(4-Fluoro-phenoxy)-benzene sulfonylamino]-3,3-dimethyl-pent-4-enoic acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyric acid;

2-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-3-methyl-3-(5-methyl-isoazole-3-ylmethylsulfanyl)-butyric acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyramide;

2-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyramide;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(carbomethoxyethylsulfanyl)-butyric acid;

1-[2-(Benzothiazol-2-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(hydroxyethylsulfanyl)-butyric acid;

[4-Methoxy-benzenesulfonylamino]-3-methyl-3-(pyridin-2-yl-sulfanyl)-butyric acid;

N-(4,4-Dimethyl-2-oxo-tetrahydro-furan-3S-yl)-3R-[1-(4′-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(amidoethylsulfanyl)-butyric acid;

[4-Methoxy-benzenesulfonylamino]-3-methyl-3-(pyridin-2-ylsulfanyl)-butyric acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3,3-dimethyl-5-phenyl-pent-4-enoic acid;

5-[4-(4-Fluoro-phenoxy)-benzenesulfonyl]-4,5,6,7-tetrahydro-3H-imidazole[4,5,-c]pyridine-6-carboxylic acid hydroxyamide

2(R)-[4-(4-Methylphenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid;

3(S)-4-(4-((Pyrid-4-yl)oxy)benzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxylic acid;

1-[4-(Pyridin-4-ylsulfanyl)-piperidine-1-sulfanyl]-piperidine-2-carboxylic acid hydroxyamide;

N-[1-(1H-imidazol-2-yl)-3-methyl-butyl]-3-[1-(4′-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

3R-{3-[(4-Cyano-phenyl)-acetyl]-pyrrol-1-yl}-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid;

1-[4-(4-Methoxy-phenylsulfamyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid methyl ester;

2(R)-[4-(4-Methylphenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid, hydroxyamide;

1-[4-(4-Methyl-phenylsulfamyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

4-(4-Methoxy-benzenesulfonyl)-2,2-dimethyl-thiomorpholine-3-carboxylic acid;

4-4(-Methoxy-benzenesulfonyl)-2,2-dimethyl-thiomorpholine-3-carboxylic acid hydroxyamide;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid hydroxyamide;

2(R)-[4-(4-bromo-phenoxy)benzenesulfoxylamino]-3-methyl-3-(pyridi-n-yl-sulfuroxide)butyric acid, hydroxyamide;

4-(4-Methoxy-bezensulfonyl)-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

2,2-Dimethyl-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]thiomorpholin-3-ol;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethoxy-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

2-(R)-3-Methyl-3-(pyridin-2-yl-sulfanyl)-[4-(4-trifluoromethylphenoxy)-benzenesulfonylamino]-butyric acid;

3(R)-4-(4-(Pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

2R-3-Methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-oxy)-benzenesulfonylamino]-butyric acid;

2R-N-Hydroxy-3-methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-oxy)-benzenesulfonylamino]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-3-hydroxy-3-methyl-butyric acid;

3(S)-2,2-Dimethyl-4-[4-(pyridin-4-ylsulfanyl)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid hydroxyamide;

2R-3-Methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-sulfanyl)-benzenesulfonylamino]-butyric acid;

2R-N-Hydroxy-3-methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-sulfanyl)-benzenesulfonylamino]-butyramide;

3,3-Dimethyl-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyric acid;

3,3-Dimethyl-N-hydroxy-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-[(1-methyl-imidazol-2-yl)methylsulfanyl]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-3-methyl-3-[(1-methyl-imidazol-2-yl)methylsulfanyl]-butyric acid;

N-Hydroxy-2-[(4-methylbenzenesulfonyl)amino]acetamide;

1-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

1-[4-(4-Imidazol-1-yl-phenylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-Chloro-benzoyl)-cyclohexanesulfonyl]-piperidine-1-carboxylic acid hydroxyamide;

1(R)-[4-(4-Chloro-benzoyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid amide;

1(R)-(4-Pyridin-2-yl-piperazine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1(R)-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid;

1(R)-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]- piperidine-2-carboxylic acid hydroxyamide;

N-Hydroxy-3,3-dimethyl-2R-[4-(morpholine-4-carbonyl)piperidine-1-sulfonylamino]butyramide;

N-Hydroxy-3-methyl-3-(5-methyl-isoxazol-3-yl-methylsulfanyl)-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-sulfonylamino]-butyramide;

4-(4′-Chloro-biphenyl-4-yl)-2RS-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-oxo-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-2R-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-oxo-butyric acid;

N-Hydroxy-2R-[4-(4-imidazol-1-yl-phenoxy)-piperidine-1-sulfonylamino]-3,3-dimethyl-butyramide;

2R-[4-(4-Chloro-benzoyl)-piperazine-1-sulfonylamino]-N-hydroxy-3-methyl-3-methylsulfanyl-butyramide;

N-Hydroxy-3-methyl-3-methylsulfanyl-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyramide;

4-(Pyridin-4-yloxy)benzenesulfonic acid;

4-(Pyridin-4-yloxy)benzenesulfonyl chloride hydrochloride;

(3S)-2,2-Dimethyl-3-thiomorpholine carboxylic acid;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-1,1-dioxo-tetrahydro-2H-1,4-thiazine-3-carboxamide;

1R-3S-2,2-Dimethyl-1-oxo-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]-1-thiomorpholine-3-carboxylic acid amide;

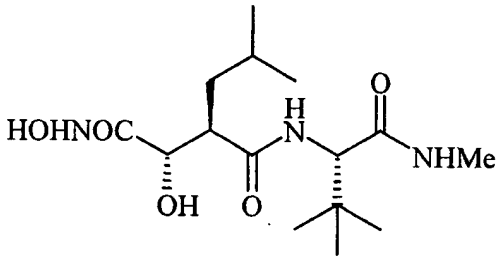
1S-3S-2,2-Dimethyl-1-oxo-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]-1-thiomorpholine-3-carboxylic acid amide; and

4-[4-(1-Hydroxy-pyridin-4-yloxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid amide.

Especially preferred are the MMP inhibitors currently in clinical development, for example batimastat (**2**).

MMP compounds in clinical development include batimastat (**2**) for the treatment of malignant pleural effusion, and marimastat (**1**) for the treatment of pancreatic cancer. Galardin (**3**) is for the treatment of corneal ulcers, and a specific MMP-1 inhibitor is RO 31-9790 (**4**).

Compounds in Clinical Development



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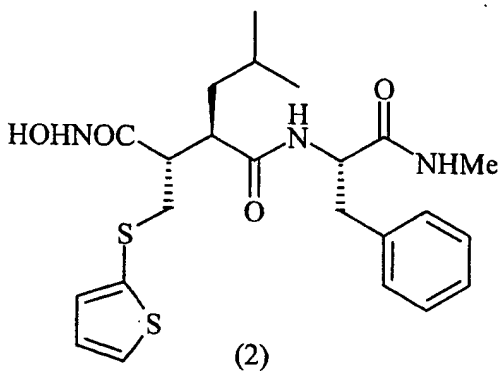

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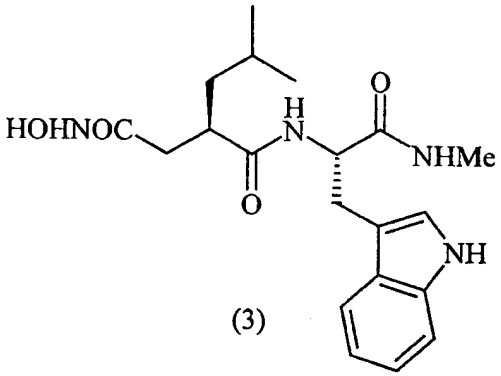

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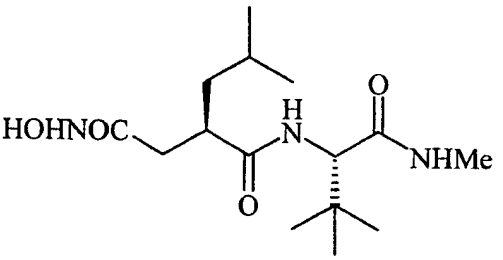


(4)

All that is required to practice the present invention is to administer to a mammal suffering from atherosclerosis, an effective amount of a matrix metalloproteinase inhibitor and an ACAT inhibitor. Compounds which can inhibit the actions of matrix metalloproteinase enzymes can be identified utilizing routine in vitro and in vivo assays. Several compounds from within the foregoing classes have been evaluated in such standard assays and determined to be potent matrix metalloproteinase inhibitors. The assays measure the amount by which a test compound reduces the hydrolysis of a thiopeptolide substrate caused by a matrix metalloproteinase enzyme. Such assays are described in detail by Ye, et al., in Biochemistry, Vol. 31, No 45, 1992, (11231-11235), which is incorporated herein by reference.

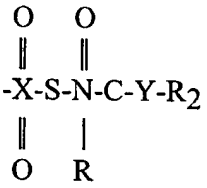
Thiopeptolide substrates show virtually no decomposition or hydrolysis in the absence of a matrix metalloproteinase enzyme. A typical thiopeptolide substrate commonly utilized for assays is Ac-Pro-Leu-Gly-thioester-Leu-Leu-Gly-O Et. A 100 µL assay mixture will contain 50 mM of 2-morpholinoethane sulfonic acid monohydrate (MES, pH 6.0) 10 mM $CaCl_2$, 100 µM thiopeptolide

substrate, and 1 mM 5,5′-dithio-bis-(2-nitro-benzoic acid) (DTNB). The thiopeptolide substrate concentration is varied from 10 to 800 μM to obtain Km and Kcat values. The change in absorbance at 405 nm is monitored on a Thermo Max microplate reader (molecular Devices, Menlo Park, CA) at room temperature (22°C). The calculation of the amount of hydrolysis of the thiopeptolide substrate is based on $E_{412} = 13600\ m^{-1}\ cm^{-1}$ for the DTNB-derived product 3-carboxy-4-nitrothiophenoxide. Assays are carried out with and without matrix metalloproteinase inhibitor compounds, and the amount of hydrolysis is compared for a determination of inhibitory activity of the test compounds.

Several representative compounds have been evaluated for their ability to inhibit various matrix metalloproteinase enzymes. Table I below presents inhibitory activity for compounds from various classes. In the table, MMP-1 refers to interstitial collagenase; MMP-2 refers to Gelatinase A; MMP-3 refers to stromelysin; MMP-7 refers to matrilysin; and MMP-9 refers to Gelatinase B. Test compounds were evaluated at various concentrations in order to determine their respective IC_{50} values, the micromolar concentration of compound required to cause a 50% inhibition of the hydrolytic activity of the respective enzyme.

As noted above, any matrix metalloproteinase inhibitor can be used to treat or prevent atherosclerotic lesions according to this invention.

ACAT inhibitors useful in the practice of the instant invention are those of Formula I



I

or a pharmaceutically acceptable salt thereof wherein:

X and Y are selected from oxygen, sulfur and $(CR'R'')_n$ wherein n is an integer of from 1 to 4 and R′ and R′ are each independently hydrogen, alkyl, alkoxy, halogen, hydroxy, acyloxy, cycloalkyl, phenyl optionally substituted or R′ and R″ together form a spirocycloalkyl or a carbonyl;

R is hydrogen, a straight or branched alkyl of from 1 to 8 carbon atoms or benzyl;

R_1 and R_2 are each independently selected from

(a) phenyl or phenoxy each of which is unsubstituted or is substituted with 1 to 5 substituents selected from

phenyl,

an alkyl group having from 1 to 6 carbon atoms and which is straight or branched,

an alkoxy group having from 1 to 6 carbon atoms and which is straight or branched;

phenoxy,

hydroxy,

fluorine,

chlorine,

bromine,

nitro,

trifluoromethyl,

-COOH,

-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched,

$-(CH_2)_pNR_3R_4$ wherein p is zero or one, and each of R_3 and R_4 is selected from hydrogen or a straight or branched alkyl group having 1 to 4 carbon atoms;

(b) 1- or 2-naphthyl unsubstituted or substituted with from 1 to 3 substituents selected from

phenyl,

an alkyl group having from 1 to 6 carbon atoms and which is straight or branched,

an alkoxy group having from 1 to 6 carbon atoms and which is straight or branched;

hydroxy,

phenoxy,

fluorine,

chlorine,

bromine,

nitro,

trifluoromethyl,

-COOH,

-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched,

$-(CH_2)_pNR_3R_4$ wherein p, R_3 and R_4 have the meanings defined above;

(c) arylalkyl;

(d) a straight or branched alkyl chain having from 1 to 20 carbon atoms and which is saturated or contains from 1 to 3 double bonds; or

(e) adamantyl or a cycloalkyl group wherein the cycloalkyl moiety has from 3 to 6 carbon atoms.

Preferred compounds of the instant invention are those of Formula I:

wherein R_1 is phenyl or is phenyl disubstituted in the 2,6-positions,

wherein R_2 is phenyl or is phenyl disubstituted in the 2,6-positions,

wherein each of R_1 and R_2 is phenyl,

wherein each phenyl is disubstituted in the 2,6-position,

wherein R_1 is phenyl disubstituted in the 2,6-positions and R_2 is phenyl trisubstituted in the 2,4,6-positions,

wherein R_1 is 2,6-bis(1-methylethyl)phenyl and R_2 is 2,6-bis(1-methylethyl)phenyl or 2,4,6-tris(1-methylethyl)phenyl,

wherein one of R_1 and R_2 is the group

$$-(CH_2)_t-\underset{\displaystyle R_6}{\overset{\displaystyle R_5}{\overset{|}{\underset{|}{C}}}}-(CH_2)_w-R_7\,,$$

wherein t is zero or 1 to 4;

w is zero or 1 to 4 with the proviso that the sum of t and w is not greater than 5;

R_5 and R_6 are each independently selected from hydrogen or alkyl having from 1 to 6 carbon atoms, or when R_5 is hydrogen, R_6 can be selected from the groups defined for R_7; and

R_7 is phenyl or phenyl substituted with from 1 to 3 substituents selected from a straight or branched alkyl group having from 1 to 6 carbon atoms, straight or branched alkoxy group having from 1 to 6 carbon atoms, phenoxy, hydroxy, fluorine, chlorine, bromine, nitro, trifluoromethyl, -COOH, COOalkyl wherein alkyl has from 1 to 4 carbon atoms, or $-(CH_2)_pNR_3R_4$ wherein P, R_3 and R_4 have the meanings defined above.

Also preferred compounds of the instant invention are those of Formula I wherein

X is oxygen, sulfur or $(CR'R'')_n$;

Y is oxygen, sulfur or $(CR'R'')_n$, with the proviso that at least one of X or Y is $(CR'R'')_n$ wherein n is an integer of from 1 to 4 and R′ and R″ are each independently hydrogen, straight or branched alkyl of from 1 to 6 carbons, optionally substituted phenyl, halogen, hydroxy, alkoxy, acyloxy, cycloalkyl, or R′ and R″ taken together form a carbonyl or a spirocycloalkyl group of from 3 to 10 carbons;

R is hydrogen;

R_1 is phenyl optionally substituted, straight or branched alkyl of from 1 to 10 carbon atoms, cycloalkyl of from 3 to 10 carbon atoms;

R_2 is phenyl optionally substituted, straight or branched alkyl of from 1 to 10 carbon atoms, cycloalkyl of from 3 to 8 carbon atoms, phenoxy optionally substituted with the proviso that only if X is $(CR'R'')_n$ can R_1 be optionally substituted phenoxy and only if Y is $(CR'R'')_n$ can R_2 be optionally substituted phenoxy, and with the further proviso that at least one of R_1 and R_2 is optionally substituted phenyl or phenoxy.

More preferred compounds of the instant invention are those of Formula I wherein

X is oxygen;

Y is $(CR'R'')_n$ wherein n is an integer of from 1 to 2;

R is hydrogen;

R_1 is optionally substituted phenyl;

R_2 is optionally substituted phenyl or phenoxy, straight or branched alkyl of from 1 to 10 carbons, or cycloalkyl of from 3 to 10 carbons; and

R′ and R″ are each independently hydrogen, straight or branched alkyl of from 1 to 6 carbons, optionally substituted phenyl, halogen, hydroxy, alkoxy, acyloxy, cycloalkyl, or R′ and R″ taken together form a carbonyl or a spirocycloalkyl.

Preferred compounds of Formula I include, but are not limited to the following:

Sulfamic acid (phenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid[[2,4,6-tris(1-methylethyl)phenyl]acetyl-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl-2,4,6-tris(1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,4,6-tris(1-methylethyl)phenyl ester,

Sulfamic acid[adamantaneacetyl]-2,6-bis[1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester-sodium salt,

Sulfamic acid[[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester-sodium salt,

Sulfamic acid (decanoyl)-2,6-bis-(1-methylethyl)phenyl ester,

Sulfamic acid (dodecanoyl)-2,6-bis-(1-methylethyl)phenyl ester,

2,6-Bis(1-methylethyl)-N-[[[2,4,6-tris(1-methylethyl)phenyl]methyl]-sulfonyl]benzeneacetamide,

2,6-Bis(1-methylethyl)-N-[[[2,4,6-tris(1-methylethyl)phenyl]methyl]-sulfonyl]benzeneacetamide-sodium salt,

2,6-Bis(1-methylethyl)phenyl[[[2,4,6-tris(1-methylethyl)phenyl]methyl]-sulfonyl]carbamate,

2,6-Bis(1-methylethyl)phenyl[[[2,4,6-tris(1-methylethyl)phenyl]methyl]-sulfonyl]carbamate-sodium salt,

Sulfamic acid (1-oxo-3,3-diphenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,6-dichlorophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,6-dichlorophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid trans-[(2-phenylcyclopropyl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,5-dimethoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,4,6-trimethoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,4,6-trimethylphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-thiophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [3-thiophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-methoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (oxophenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-trifluoromethylphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2-phenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclopentylphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclohexylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (diphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (triphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(1-phenylcyclopentyl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (3-methyl-1-oxo-2-phenylpentyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2-phenylbutyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclohexylphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2,2-diphenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(9H-fluoren-9-yl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-3-phenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [1-oxo-3-[2,4,6-tris(1-methylethyl)phenyl]-2-propenyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [1-oxo-3-[2,4,6-tris(1-methylethyl)phenyl]propyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(acetyloxy)[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [hydroxy[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [fluoro[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (3-methyl-1-oxo-2-phenylpentyl)-2,6-bis(1-methylethyl)phenyl ester sodium salt,

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenoxy]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [[2,6-bis(1-methylethyl)phenoxy]acetyl]-2,6-bis(1-methylethyl)phenyl ester, and

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(phenyl)phenyl ester.

Other ACAT inhibitors useful in the practice of this invention are selected from:

4-Hexadecylamino-benzoic acid monosodium salt;

3,5-Dimethyl-1-[5-(1,4,5-triphenyl-2H-imidazol-2-ylsulfanyl)-pentyl]-1H-pyrazole monosodium salt;

8-(1,4,5-Triphenyl-2H-imidazol-2-yloxy)-octanoic acid;

9-Bromo-6,11-dihydro-dibenzo[b,e]oxepine-11-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

5-((3,5-Di-tert-butyl-4-hydroxy-phenylamino)-{[4-(2,2-dimethyl-propyl)-benzyl]-hexyl-amino}-methylene)-2,2-dimethyl-[1,3]dioxane-4,6-dione;

3-(2,4-Difluoro-phenyl)-1-[4-(2,2-dimethyl-propyl)-benzyl]-1-heptyl-urea;

1-Heptyl-1-[4-(3-methyl-butyl)-benzyl]-3-(2,4,6-trifluoro-phenyl)-urea;

3-(2,4-Difluoro-phenyl)-1-[5-(4,5-diphenyl-1H-imidazol-2-ylsulfanyl)-pentyl]-1-heptyl-urea;

1-Butyl-3-{2-[3-(5-ethyl-4-phenyl-imidazol-1-yl)-propoxy]-6-methyl-phenyl}-urea;

1-(2-{2-[4-(2,2-Dimethyl-propyl)-phenyl]-ethyl}-4,6-difluoro-phenyl)-3-heptyl-urea;

Octadeca-9,12-dienoic acid (1-phenyl-ethyl)-amide;

3-(1H-Indol-3-yl)-2-octadec-9-enoylamino-propionic acid ethyl ester;

3-(Dimethyl-nonyl-silanyl)-N-(1-phenyl-2-p-tolyl-ethyl)-propionamide;

(R)2-Hexyl-decanoic acid (6-methyl-2,4-bis-methylsulfanyl-pyridin-3-yl)-amide;

N-[2-(3,5-Di-tert-butyl-4-hydroxy-phenyl)-ethyl]-4-fluoro-benzenesulfonamide;

2-(2-Ethoxy-ethylsulfanyl)-4,5-diphenyl-1H-imidazole;

4-Cyano-N-[2-(4-cyano-phenyl)-3-methyl-5,5-bis-trifluoromethyl-4,5-dihydro-3H-imidazol-4-yl]-N-methyl-benzamide;

1-{3-[3-(1-Methyl-1H-imidazol-2-yl)-2-phenethyl-2H-chromen-6-yloxy]-propyl}-cyclopentanecarboxylic acid ethyl ester;

1-[4-(2-Chloro-phenyl)-2-ethyl-thieno[2,3-b]pyridin-5-yl]-3-(2,4-difluoro-phenyl)-urea;

1-(2-Cyclohexyl-[1,3]dithiolan-2-ylmethyl)-3-(2,6-diisopropyl-phenyl)-urea;

1-Cycloheptyl-1-(2,3-dihydro-benzo[1,4]dioxin-5-ylmethyl)-3-(2,4,6-trimethyl-phenyl)-urea;

1-{2-[4-(1,2-Dimethoxy-ethoxy)-phenyl]-ethyl}-3-(2,4-dimethoxy-phenyl)-1-heptyl-urea;

2-(4-{2-[3-(2,4-Dimethoxy-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-methyl-propionic acid;

3-(2,4-Difluoro-phenyl)-1-octyl-1-(2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl)-urea;

N-(2,6-Diisopropyl-phenyl)-2-octadecylsulfanyl-acetamide;

2-Bromo-6,11-dihydro-dibenzo[b,e]oxepine-11-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

(±)N-(1,2-Diphenyl-ethyl)-3-(2-heptyloxy-phenyl)-propionamide;

2,2-Dimethyl-dodecanoic acid (7-methoxy-4-oxo-chroman-8-yl)-amide;

(Z)1-(6,7-Dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-octadec-9-en-1-one;

(Z)2,2,5,5-Tetramethyl-[1,3]dioxane-4-carboxylic acid [2-(2-octadec-9-enoylamino-ethylcarbamoyl)-ethyl]-amide;

1-Benzyl-1-(5-methyl-3-phenyl-benzofuran-2-ylmethyl)-3-(2,4,6-trifluoro-phenyl)-urea;

5-Chloro-3-o-tolyl-benzofuran-2-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

2-(2,4a-Dimethyl-4a,5-dihydro-naphthalen-1-ylsulfanyl)-N-{2-[(6,6-dimethyl-hepta-2,4-diynyl)-pentyl-amino]-ethyl}-acetamide;

(Z)Octadec-9-enoic acid [2-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)-1-phenyl-ethyl]-amide;

N-(4-Dihexylamino-6-mercapto-2-methyl-pyrimidin-5-yl)-4-(phenyl-propyl-amino)-butyramide;

(Z)1-(6,7-Dimethoxy-3-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-octadec-9-en-1-one;

(trans)1,4-Bis-(4-methoxy-phenyl)-3-(3-phenyl-propyl)-azetidin-2-one;

1-Butyl-3-{2-dimethylamino-6-[3-(4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-urea;

1-{2-Dimethylamino-6-[3-(4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-3-pentyl-urea;

1-{2-Dimethylamino-6-[3-(5-methyl-4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-3-pentyl-urea;

1-(2-{2-[4-(2,2-Dimethyl-propyl)-phenyl]-ethyl}-4,6-difluoro-phenyl)-3-heptyl-urea;

(4S-trans)6-(4,5-Diphenyl-1H-imidazol-2-ylsulfanylmethyl)-4-hydroxy-4-methyl-tetrahydro-pyran-2-one;

2-(3-[1,3]Dioxan-2-yl-propylsulfanyl)-4,5-diphenyl-1H-imidazole;

Hydroxy-phenyl-acetic acid 3,3,5-trimethyl-cyclohexyl ester;

Acetic acid 1-(11-hydroxy-4-methoxy-9-methyl-5-oxo-5H,7H-6,12-dioxa-dibenzo[a,d]cycloocten-3-yl)-3-methyl-butyl ester;

10-Hydroxy-2,4a,6a,6b,9,10,12a-heptamethyl-4-octadecanoyloxy-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10, 11,12,12a,12b,13,14b-eicosahydro-picene-2-carboxylic acid;

3-[(2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-propionic acid 2-[3-(2,2-dimethyl-propyl)-3-nonyl-ureido]-cyclohexyl ester;

1-(2,6-Diisopropyl-phenyl)-3-(2-p-tolyl-heptyl)-urea;

1-[4-(2-Chloro-phenyl)-6,8-dimethyl-quinolin-3-yl]-3-(2,4-difluoro-phenyl)-urea;

1-[4-(2-Chloro-phenyl)-1,6,7-trimethyl-2-oxo-1,2-dihydro-quinolin-3-yl]-3-(2,4-difluoro-phenyl)-urea;

1-[4-(2-Chloro-phenyl)-6,7-dimethyl-2-oxo-2H-chromen-3-yl]-3-(2,4-difluoro-phenyl)-urea;

(S)1-[6-Bromo-5-(2-chloro-phenyl)-1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[e][1,4]diazepin-7-yl]-3-(2-hydroxy-1-hydroxymethyl-1-methyl-ethyl)-urea;

3-(4,5-Diphenyl-1H-imidazol-2-ylsulfanylmethyl)-1-methyl-piperidine;

2-(5,5-Dimethyl-[1,3]dioxan-2-yl)-4,5-diphenyl-1H-imidazole;

2,2-Dimethyl-5-[3-(1-methyl-1H-imidazol-2-yl)-2-propyl-chroman-6-yloxy]-pentanoic acid ethyl ester;

N-(4-Hexadecylamino-benzoyl)-4-methyl-benzenesulfonamide;

2-(4-Chloro-phenyl)-6-cyclohexyl-4-(2-oxo-2-phenyl-ethyl)-6,7-dihydro-4H-1,4,6,8a-tetraaza-s-indacene-5,8-dione;

[2-(3-tert-Butyl-4-hydroxy-naphthalen-1-yl)-1-(diethoxy-phosphoryl)-vinyl]-phosphonic acid diethyl ester;

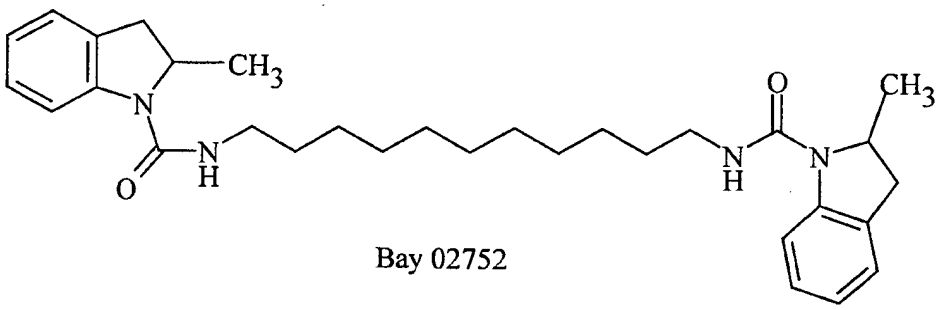
5-[1-(acetyloxy)-3-methylbutyl]-2′-(hydroxymethyl)-4-methoxy-4′-methylspiro[benzofuran-2(3H),1′-cyclohexa-2′,4′-diene]-3,6′-dione;

5-[1-(acetyloxy)-3-methylbutyl]-4-methoxy-4′-methyl-3,6-dioxospiro[benzofuran-2(3H),1′-cyclohexa-2′,4′-diene]-2′-carboxaldehyde;

(3α,4α,22α,24α)-3-hydroxy-22-[(1-oxooctadecyl)oxy]-24-norolean-12-en-29-oic acid;

1-[5-(4,5-Diphenyl-1H-imidazole-2-sulfinyl)-pentyl]-3,5-dimethyl-1H-pyrazole; and

N-butyl-3-[[(4-decyloxyphenyl)carbonyl]amino]-4-(methylthio)-benzamide;



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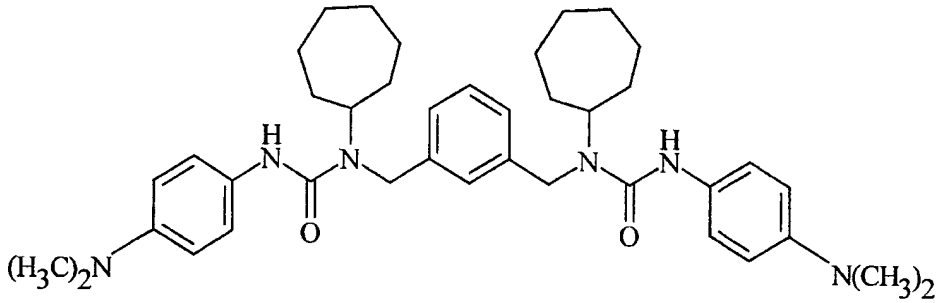

; and

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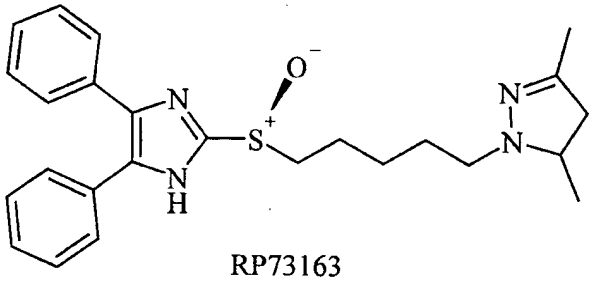

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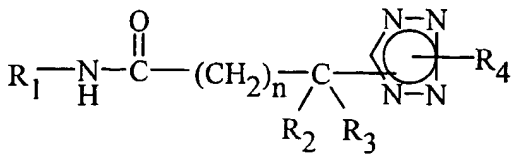
The compounds, both ACAT and MMP inhibitors, include all possible stereoisomers.

METHODS

The direct antiatherosclerotic potential of ACAT and MMP inhibitors is evaluated in a model of atherosclerotic lesion regression. Male New Zealand White rabbits (Kuiper Farms, Gary, Indiana) weighing 1.2 to 1.5 kg are meal-fed a chow diet (Purina 5321) supplemented with 0.5% cholesterol (C), 3% peanut (PNO) oil, and 3% coconut (CNO) oil diet for a total of 9 weeks followed by a 0% C, 3% PNO, and 3% CNO diet (chow/fat diet) for 6 weeks prior to an 8-week administration of the ACAT inhibitor, for example, sulfamic acid[[2,4,6-tris-(1-methylethyl)phenyl]acetyl-2,6-bis(1-methylethyl)phenyl ester, the HMG-CoA reductase inhibitor, for example, simvastatin, either alone or together. The dietary regimen consists of feeding 30 g for the first week, 40 g for 2 weeks, 50 g for 2 weeks, 60 g for 4 weeks, 70 g for the next 6 weeks, and 80 g for the final 8 weeks. After 1 week of diet initiation, a chronic endothelial injury is induced in the abdominal aorta and femoral artery by surgically inserting a sterile, indwelling, 18-cm nylon monofilament with a diameter of 200 μM into the lumen of the right femoral artery. After the initial 15-week lesion induction phase, which consists of both a hypercholesterolemic and plasma cholesterol normalization stage, the animals are randomized on the basis of their 24-hour postmeal plasma total cholesterol values into groups which are not statistically different. A group of animals, termed the time zero control (n = 16), is necropsied prior to drug administration while a second group, termed the progression control (n = 16), is maintained on the chow/fat diet for the remaining 8 weeks of the study. Additional groups of animals are administered either ACAT inhibitors, MMP inhibitors, or coadministered both compounds.

Other ACAT inhibitors useful in the practice of the instant invention are those of Formula 1 below



wherein n is zero, one or two;

wherein R_1 is selected from

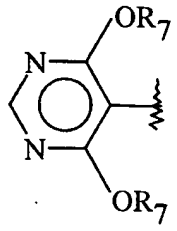
(a) phenyl which is unsubstituted or is substituted with from one to three substituents selected from:
alkyl having from 1 to 4 carbon atoms and which is straight or branched,
alkoxy having from 1 to 3 carbon atoms and which is straight or branched,
alkylthio having from 1 to 3 carbon atoms and which is straight or branched,
hydroxy,
phenyl,
fluorine,
chlorine,
bromine,
nitro,
cyano,
trifluoromethyl,
-COOH,
-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and which is straight or branched,
$-(CH_2)_mNR_5R_6$ wherein m is zero or one, and each of R_5 and R_6 is hydrogen or a straight or branched alkyl group having 1 to 4 carbon atoms;

(b) 1- or 2-naphthyl which is unsubstituted or substituted with 1 to 3 substituents selected from:
alkyl having from 1 to 4 carbon atoms and which is straight or branched,
alkoxy having from 1 to 3 carbon atoms and which is straight or branched,
hydroxy,
fluorine,
chlorine,
bromine,
nitro,
cyano,
trifluoromethyl,
-COOH,

-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched,

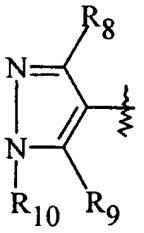
$-(CH_2)_mNR_5R_6$ wherein m, R_5, and R_6 have the meanings defined above;

(c) the group



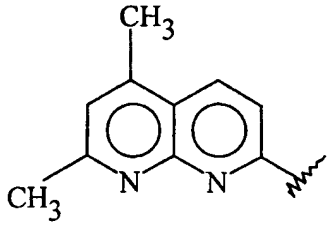
wherein R_7 is a lower alkyl group having from 1 to 3 carbon atoms and is straight or branched;

(d) the group



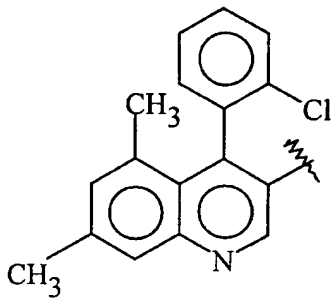
wherein R_8 and R_9 are straight or branched alkyl having from 1 to 4 carbon atoms or phenyl, and R_{10} is a straight or branched hydrocarbon group having from 1 to 18 carbon atoms which is saturated or is unsaturated containing one double bond or two nonadjacent double bonds; phenyl; phenyl substituted with from one to three substituents selected from straight or branched alkyl having 1 to 4 carbon atoms, straight or branched alkoxy having from 1 to 3 carbon atoms, hydroxy, fluorine, chlorine, bromine, nitro, cyano, trifluoromethyl, -COOH, -COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched or $-(CH_2)_mNR_5R_6$ wherein m, R_5, and R_6 are as defined above; or a heterocyclic group selected from 2-, 3-, or 4-pyridyl, 2-, 4-, or 5-pyrimidinyl, 2- or 3-pyrazinyl, 2-, 3-, 4-, 5-, 6-, 7-, or 8-quinolinyl, or 3- or 4-pyridazinyl and the N-oxides thereof;

(e) the group



;

(f) the group



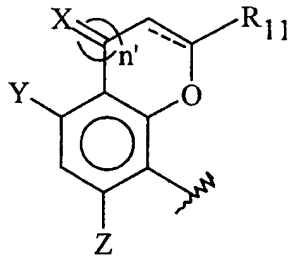
;

(g) a straight or branched hydrocarbon group having from 1 to 18 carbon atoms which is saturated or is unsaturated containing one double bond or two nonadjacent double bonds;

(h) a cycloalkyl group having from 3 to 8 carbon atoms;

(i) a heteroaromatic group selected from 2-, 3-, or 4-pyridyl which is unsubstituted or substituted with an alkyl group having from 1 to 4 carbon atoms or 2-, 4-, or 5-pyrimidinyl, and the N-oxides thereof;

(j) the group

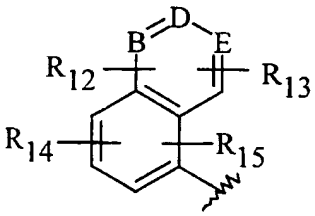


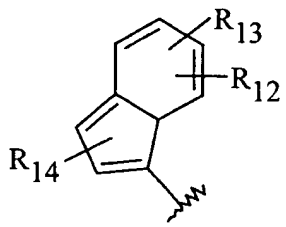
wherein --- denotes a single or double bond; Y and Z are each independently hydrogen, a straight or branched alkyl group of 1 to 4 carbon atoms, an alkoxy group of 1 to 3 carbon atoms or halo;

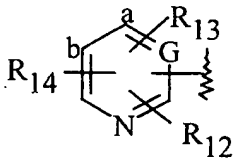
X is oxygen or two hydrogen atoms;

R_{11} is hydrogen or a straight or branched alkyl group of 1 to 4 carbon atoms, and n′ is zero or one; or

(k) is selected from the group





and 

wherein R_{12}, R_{13}, R_{14}, and R_{15} are each independently hydrogen, halo, a straight or branched alkyl group of 1 to 4 carbon atoms, an alkoxy group of 1 to 3 carbon atoms, and alkylthio group of 1 to 3 carbon atoms, cycloaklylthio of five to seven carbon atoms, phenylalkylthio in which alkyl is 1 to 4 carbon atoms, substituted phenylthio, heteroarylthio, or heteroaryloxy; and B, D, E, and G are nitrogen or carbon where one or more of B, D, and E is nitrogen; with the proviso that when G = nitrogen the group is attached to the nitrogen atom of Formula I at the 4- or 5-position of the pyrimidine ring (a and b);

wherein R_2 and R_3 are the same or different and are selected from:

(a) hydrogen, halo or one of R_2 or R_3 is hydroxy;

(b) a straight or branched alkyl group having from 1 to 12 carbon atoms, or a cycloalkyl group having from 3 to 8 carbon atoms;

(c) a phenyl or phenylalkyl group where alkyl is from 1 to 4 carbon atoms and which the phenyl ring unsubstituted or substituted with from 1 to 3 substituents selected from straight or branched alkyl having from 1 to 4 carbon atoms, straight or branched alkoxy having from 1 to 4 carbon atoms, alkythio, straight or branched having 1 to 4 carbon atoms, hydroxy, fluorine, chlorine, bromine, trifluoromethyl, cyano, nitro, phenyl, or $(CH_2)_mNR_5R_6$ wherein m, R_5, and R_6 have the meanings defined above;

(d) a straight or branched alkenyl group having from 2 to 6 carbon atoms; or

(e) R_2 and R_3 taken together with the carbon atom to which they are attached form an alkylidene group of 1 to 4 carbon atoms, a benzylidene or a spiroalkyl group having from 3 to 7 carbon atoms; or

(f) when R_2 is hydrogen, F, alkyl of C_{1-12} atoms, R_3 is a heteroaryl selected from a 5- or 6-membered monocyclic or fused bicyclic heterocyclic group containing at least 1 to 4 heteroatoms in at least one ring, said heteroatoms being nitrogen, oxygen, or sulfur and combinations thereof, said heterocyclic group being unsubstituted or substituted with an alkyl group having from 1 to 4 carbon atoms and the N-oxides thereof;

(g) 1- or 2-naphthyl which is unsubstituted or substituted with 1 to 3 substituents selected from:

alkyl having from 1 to 4 carbon atoms and which is straight or branched,

alkoxy having from 1 to 3 carbon atoms and which is straight or branched,

wherein R_4 is a straight or branched hydrocarbon chain having from 1 to 20 carbon atoms and is saturated or is unsaturated and has 1 double bond or has 2 nonadjacent double bonds or is alkylthio having 1 to 20 carbon atoms and is saturated; or a pharmaceutically acceptable salt or individual enantiomeric isomer thereof.

Specifically,the following compounds are useful in the instant invention:

N-[2,6-Bis(1-methylethyl)phenyl]-2-dodecyl-2H-tetrazole-5-acetamide;

2-Dodecyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

N-(2,4-Difluorophenyl)-2-dodecyl-2H-tetrazole-5-acetamide;

2-Tetradecyl-N-(2,4,6-tri-methoxyphenyl)-2H-tetrazole-5-acetamide;

N-(4,6-Dimethoxy-5-pyrimidinyl)-2-dodecyl-2H-tetrazole-5-acetamide;

N-(4,6-Dimethoxy-5-pyrimidinyl)-2-dodecyl-1H-tetrazole-5-acetamide;

2-Dodecyl-N-(3-methyl-2-pyridinyl)-2H-tetrazole-5-acetamide;

2-Dodecyl-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)-2H-tetrazole-5-acetamide;

1-Dodecyl-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)-1H-tetrazole-5-acetamide;

(±) 2-Dodecyl-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±) 2-Dodecyl-N,α-diphenyl-2H-tetrazole-5-acetamide;

(±)-N-[2,6-bis(1-Methylethyl)phenyl]-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-N-(2,4-Difluorophenyl)-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Octyl-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-2-Hexadecyl-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-N-(4,6-Dimethoxy-5-pyrimidinyl)-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-N-(5,7-Dimethyl-1,8-naphthyridine-2-yl)-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-phenyl-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)-2H-tetrazole-5-acetamide;

(±)-N-Cyclopropyl-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-phenyl-N-2-pyridinyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-N-(3-methyl-2-pyridinyl)-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-N-(3-methyl-2-pyridinyl)-2-phenyl-2H-tetrazole-5-acetamide, N-oxide;

(±)-N-(1,1-Dimethylethyl)-2-dodecyl-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-(2-pyridyl)-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-N-[2,6-Bis(1-methylethyl)phenyl]-2-dodecyl-α-2-pyridinyl-2H-tetrazole-5-acetamide;

2-Dodecyl-α,α-dimethyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

2-Dodecyl-α,α′-(2-propenyl)-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

1-(2-Dodecyl-2H-tetrazol-5-yl)-N-(2,4,6-trimethoxyphenyl)-yclopentanecarboxamide;

2-Tridecyl-α,α-dimethyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

2-Dodecyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-propanamide;

N-(2,6-bis(1-Methylethyl)phenyl)-2-dodecyl-2H-tetrazole-5-propanamide;

N-(2,4-Difluorophenyl)-2-dodecyl-2H-tetrazole-5-propanamide;

1-Dodecyl-N-(2,4,6-trimethoxyphenyl)-1H-tetrazole-5-propanamide;

(±)-n-(2,4-Difluorophenyl)-1-dodecyl-α-phenyl-1H-tetrazole-5-acetamide;

(±)-N-[2,6-bis(1-Methylethyl)phenyl]-1-dodecyl-α-phenyl-1H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-methyl-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-(4-fluorophenyl)-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-2-naphthalenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-α-([1,1′-Biphenyl]-4-yl)-2-dodecyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-methyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-phenylmethyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-cyclohexyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-5-acetamide;

(-)-2-Dodecyl-α-phenyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-5-acetamide $[\alpha]_D = -58°$ (1% in CH_3OH);

(+)-2-Dodecyl-α-phenyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-5-acetamide $[\alpha]_D = +55.1°$ (1% in CH_3OH);

(±)-N-[2,6-Bis(1-Methylethyl)phenyl]-2-dodecyl-α-fluoro-α-phenyl-2H-tetrazole-5-acetamide;

(±)-2-Dodecyl-α-fluoro-α-phenyl-N-(2,4,6-trimethoxy phenyl)-2H-tetrazole-5-acetamide;

N-[2,6-bis(1-Methylethyl)phenyl]-5-decyl-2H-tetrazole-2-acetamide;

N-[2,6-bis(1-Methylethyl)phenyl-5-dodecyl-2H-tetrazole-2-acetamide;

(±)-N-[2,6-bis(1-Methylethyl)phenyl]-5-dodecyl-α-phenyl-2H-tetrazole-2-acetamide;

(±)-N-[2,6-bis(1-Methylethyl)phenyl]-5-dodecyl-α-pentyl-2H-tetrazole-2-acetamide;

(±)-N-[2,6-bis(1-Methylethyl)phenyl-5-(dodecylthio)-α-phenyl-2H-tetrazole-2-acetamide;

(±)-5-Decyl-α-phenyl-N-(2,4,6-trimethoxyphenyl-2H-tetrazole-2-acetamide;

5-Dodecyl-N-(2,4,6-trimethoxy-phenyl)-2H-tetrazole-2-acetamide;

(±)-5-Dodecyl-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-2-acetamide;

(±)-5-Dodecyl-α-pentyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-2-acetamide;

(±)-N-(2,4-Difluorophenyl-5-dodecyl-α-phenyl-2H-tetrazole-2-acetamide;

5-Dodecyl-α,α-dimethyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-2-acetamide;

(±)-5-(Dodecylthio)-α-phenyl-N-(2,4,6-trimethoxyphenyl)-2H-tetrazole-2-acetamide; or

(±)-5-(Dodecylsulfinyl)-α-phenyl-N-(2,4,6)-trimethoxyphenyl)-2H-tetrazole-2-acetamide.

The compounds to be employed in the present invention can be prepared and administered in a wide variety of oral and parenteral dosage forms for treating and preventing atherosclerosis. The compounds can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Also, the compounds can be administered by inhalation, for example, intranasally. Additionally, the compounds can be administered transdermally. It will be obvious to those skilled in the art that the following dosage forms may comprise as the active component, either a compound as a free base, acid, or a corresponding pharmaceutically acceptable

salt of such compound. The active compound generally is present in a concentration of about 5% to about 95% by weight of the formulation.

For preparing pharmaceutical compositions from the compounds of the present invention, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material.

In powders, the carrier is a finely divided solid which is in a mixture with the finely divided active component.

In tablets, the active component is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

The powders and tablets preferably contain from 5% or 10% to about 70% of the active compound. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component, with or without other carriers, is surrounded by a carrier, which is thus in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges can be used as solid dosage forms suitable for oral administration.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, is first melted and the active component is dispersed homogeneously therein, as by stirring. The molten homogenous mixture is then poured into convenient sized molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, and emulsions, for example, water or water propylene glycol solutions. For parenteral injection, liquid preparations can be formulated in solution in aqueous polyethylene glycol solution.

Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizing, and thickening agents as desired.

Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well-known suspending agents.

Also included are solid form preparations which are intended to be converted, shortly before use, to liquid form preparations for oral administration. Such liquid forms include solutions, suspensions, and emulsions. These preparations may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

The pharmaceutical preparation is preferably in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

The quantity of active component in a unit-dose preparation may be varied or adjusted from 1 to 1000 mg, preferably 10 to 100 mg according to the particular application and the potency of the active component. The composition can, if desired, also contain other compatible therapeutic agents.

The compounds utilized in the pharmaceutical method of this invention are administered at a dose that is effective to inhibit the hydrolytic activity of one or more matrix metalloproteinase enzymes. Such effective amounts are thus those which prevent or treat CHF and ventricular dilatation. The compounds can also be used prophalactically at the same dose levels. The initial dosage of about 1 mg to about 100 mg per kilogram daily will be effective to prevent and treat heart failure. A daily dose range of about 5 to about 75 mg is preferred. The dosages, however, may be varied depending upon the requirements of the patient, the severity of the condition being treated, and the compound being employed.

Determination of the proper dosage for a particular situation is within the skill of the art. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstance is reached. For convenience, the total daily dosage may be divided and administered in portions during the day if desired. Typical dosages will be from about 0.1 to about 500 mg/kg, and ideally about 25 to about 250 mg/kg.

The following examples illustrate typical formulations that can be utilized in the invention.

Tablet Formulation

Ingredient	Amount (mg)
2-(4'-bromobiphenyl-4-sulfonylamino)-3-methyl-butyric acid ACAT Compound	25
Lactose	50
Corn starch (for mix)	10
Corn starch (paste)	10
Magnesium stearate (1%)	5
Total	100

The biphenylsulfonamide, lactose, and corn starch (for mix) are blended to uniformity. The corn starch (for paste) is suspended in 200 mL of water and heated with stirring to form a paste. The paste is used to granulate the mixed powders. The wet granules are passed through a No. 8 hand screen and dried at 80°C. The dry granules are lubricated with the 1% magnesium stearate and pressed into a tablet. Such tablets can be administered to a human from one to four times a day for treatment of atherosclerosis and arthritis.

Preparation for Oral Solution

Ingredient	Amount
(R)-2-(4′-Cyanobiphenyl-4-sulfonylamino)-3-phenyl-propionic acid sodium salt ACAT Compound	400 mg
Sorbitol solution (70% N.F.)	40 mL
Sodium benzoate	20 mg
Saccharin	5 mg
Red dye	10 mg
Cherry flavor	20 mg
Distilled water q.s.	100 mL

The sorbitol solution is added to 40 mL of distilled water, and the biphenylsulfonamide is dissolved therein. The saccharin, sodium benzoate, flavor, and dye are added and dissolved. The volume is adjusted to 100 mL with distilled water. Each milliliter of syrup contains 4 mg of invention compound.

Parenteral Solution

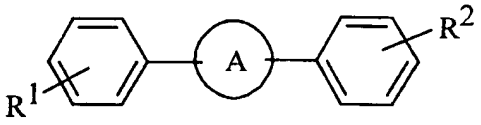
In a solution of 700 mL of propylene glycol and 200 mL of water for injection is suspended 20 g of (S)-2-(4′-amino-biphenyl-4-sulfonylamino)-3-(3-ethoxyphenyl)-propionic acid. After suspension is complete, the pH is adjusted to 6.5 with 1N sodium hydroxide, and the volume is made up to 1000 mL with water for injection. The formulation is sterilized, filled into 5.0 mL ampoules each containing 2.0 mL, and sealed under nitrogen.

CLAIMS

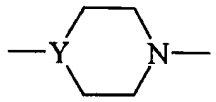
1. A method for treating and/or preventing atherosclerotic lesions in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of an ACAT inhibitor with a therapeutically effective amount of a MMP inhibitor.

2. A method for preventing plaque rupture and for promoting lesion regression in a mammal in need of said treatment and/or prevention comprising administering to said mammal a therapeutically effective amount of an ACAT inhibitor with a therapeutically effective amount of a MMP inhibitor.

3. A method according to Claim 1 utilizing a compound of the formula



wherein:

A is a bond, CONH, or  , where Y is CH or N;

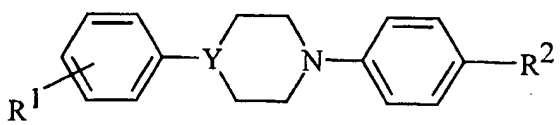
R^1 is alkyl, aryl, halo, amino, substituted or disubstituted amino, or alkoxy;

R^2 is carboxyalkyl ketone or oxime, carboxyalkylsulfonamide, or $-SO_2-NHCHCOOH$; and

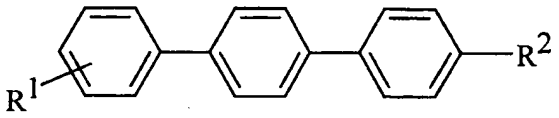
R^3

R^3 is alkyl, substituted alkyl, amino, substituted or disubstituted amino, or aryl, and pharmaceutically acceptable salts thereof.

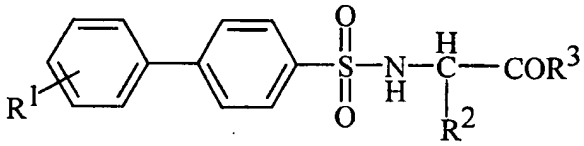
4. A method of Claim 3 utilizing a compound of the formula



5. A method according to Claim 3 employing a compound of the formula



6. A method according to Claim 4 employing a compound of the formula



wherein:

R^1 is C_1-C_6 alkyl, halo, nitro, NR^4R^5, cyano, OR^4, and $COOR^4$;

R^2 is C_1-C_6 alkyl, optionally substituted by phenyl, substituted phenyl,

NR^4R^5, OR^6, carboxy, carboxamido, H_2N-C-NH-, thio, methylthio, indole, imidazole, phthalimido, phenyl, and substituted phenyl;

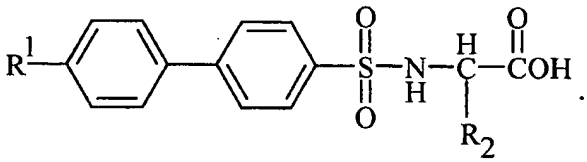
R^3 is OH, OC_1-C_6 alkyl, or NHOH;

R^4 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 alkanoyl;

R^5 is hydrogen or C_1-C_6 alkyl; and

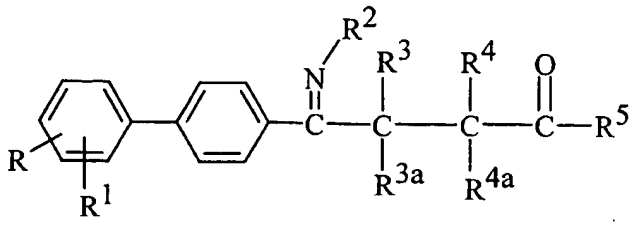
R^6 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkanoyl, phenyl, or substituted phenyl.

7. A method according to Claim 5 employing a compound of the formula



8. A method according to Claim 6 employing 2-(4′-bromobiphenyl-4-sulfonylamino)-3-methyl-butyric acid.

9. A method according to Claim 2 employing a compound of the formula



wherein R and R^1 are the same or different and are

hydrogen,

alkyl,

halogen,

nitro,

yano,

rifluoromethyl,

OR^6 wherein R^6 is hydrogen,

alkyl,

aryl,

arylalkyl,

heteroaryl, or

cycloalkyl,

$-N-R^6$ wherein R^6 and R^{6a} are the same or different and are
|
R^{6a}

as defined above for R^6,

$-O-\overset{\overset{O}{\|}}{C}-R^6$ wherein R^6 is as defined above,

$-NH-\overset{\overset{O}{\|}}{C}-R^6$ wherein R^6 is as defined above,

$-S-\overset{\overset{O}{\|}}{C}-R^6$ wherein R^6 is as defined above,

$-SR^6$ wherein R^6 is as defined above,

O
‖
-C-R^6 wherein R^6 is as defined above,

-CH_2-OR^6 wherein R^6 is as defined above,

-CH_2-N-R^6 wherein R^6 and R^{6a} are the same or different
|
R^{6a}

and are as defined above for R^6,

O
‖
-C-N-R^6 wherein R^6 and R^{6a} are the same or different and
|
R^{6a}

are as defined above for R^6,

O
‖
-S-R^6 wherein R^6 is as defined above,
‖
O

cycloalkyl, or

heteroaryl, with the proviso that R and R^1 are not both hydrogen;

R^2 is -OR^6 wherein R^6 is as defined above, or

-N-R^6 wherein R^6 and R^{6a} are the same or different and are
|
R^{6a}

as defined above for R^6;

R^3, R^{3a}, R^4, and R^{4a} are the same or different and are hydrogen,

fluorine,

alkyl,

-$(CH_2)_n$-aryl wherein n is an integer from 1 to 6,

-$(CH_2)_n$-heteroaryl wherein n is as defined above,

-$(CH_2)_n$-cycloalkyl wherein n is as defined above,

$-(CH_2)_p-X-(CH_2)_q$-aryl wherein X is O, S, SO, SO_2, or NH, and p and q are each zero or an integer of 1 to 6, and the sum of p + q is not greater than six,

$-(CH_2)_p-X-(CH_2)_q$-heteroaryl wherein X, p, and q are as defined above, or

$-(CH_2)_n-R^7$ wherein R^7 is

N-phthalimido,

N-2,3-naphthyimido,

$-OR^6$ wherein R^6 is as defined above,

$-N(R^6)(R^{6a})$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^6,

$-SR^6$ where R^6 is as defined above,

$-S(=O)-R^6$ wherein R^6 is as defined above,

$-S(=O)_2-R^6$ wherein R^6 is as defined above,

$-O-C(=O)-R^6$ wherein R^6 is as defined above,

$-N(R^{6a})-C(=O)-R^6$ wherein R^6 and R^{6a} are the same or different and are as defined above for R^6,

$-S-C(=O)-R^6$ wherein R^6 is as defined above,

-C-R^6 wherein R^6 is as defined above,

-C-OR^6 wherein R^6 is as defined above, or

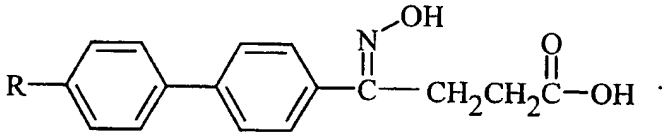
-C-N-R^6 wherein R^6 and R^{6a} are the same or different

and are as defined above for R^6, and

n is as defined above;

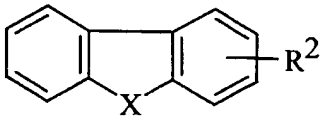
R^5 is OH or SH; with the proviso that R^3, R^{3a}, R^4, and R^{4a} are hydrogen or at least one of R^3, R^{3a}, R^4, or R^{4a} is fluorine; and corresponding isomers thereof; or a pharmaceutically acceptable salt thereof.

10. A method according to Claim 8 employing a compound of the formula



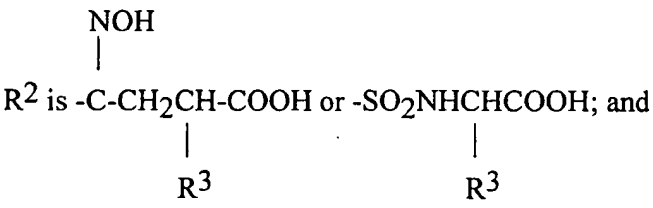
11. A method according to Claim 9 employing 4-(4′-chlorobiphenyl-4-yl)-4-hydroxyimino-butyric acid.

12. A method according to Claim 1 employing a compound of the formula



wherein

X is oxygen or -C-CH_2-

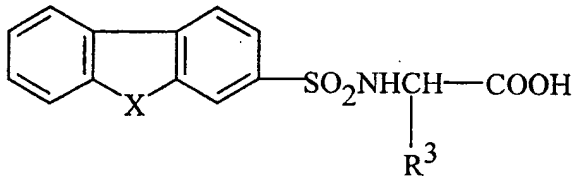


R^2 is -C-CH_2CH-COOH or -SO_2NHCHCOOH; and

R^3 R^3

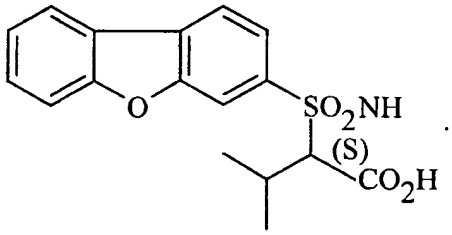
R^3 is alkyl, halo, alkoxy, acyl, or aryl.

13. A method according to Claim 11 employing a compound of the formula

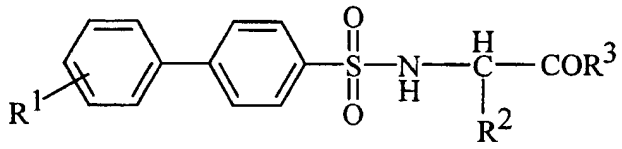


14. A method according to Claim 12 employing (S)-2-(9H-fluorene-2-sulfonylamino)-4-phenyl-butyric acid.

15. A method according to Claim 12 employing



16. A method according to Claim 1 employing a compound of formula I



wherein:

R^1 is C_1-C_6 alkyl, halo, nitro, $(CH_2)_{0-4}$-NR^4R^5,

cyano, OR^4, CH, CF_3, CNR^4R^5, and $COOR^4$;

R^2 is hydrogen or C_1-C_6 alkyl, optionally substituted by the following groups: phenyl, substituted phenyl, phenoxy, substituted phenoxy, NR^4R^5, OR^6, carboxy, carboxamido, H_2N-C(=O)-HN-, thio, methylthio, indole, imidazole, and phthalimido;

R^3 is OH, O, C_1-C_6 alkyl, or NHOH;

R^4 is hydrogen, C_1-C_6 alkyl, or C_1-C_6 alkanoyl;

R^5 is hydrogen or C_1-C_6 alkyl; and

R^6 is hydrogen, C_1-C_6 alkyl, C_1-C_6 alkanoyl, phenyl, or substituted phenyl, and pharmaceutically acceptable salts and solvates thereof.

17. A method according to Claim 1 wherein the compound employed is selected from

(S)-2-(4′-Bromo-biphenyl-4-sulfonylamino)--3-methyl-butyric acid;

(S)-2-(4′-Chloro-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-3-Methyl-2-(4′-nitro-biphenyl-4-sulfonylamino)-butyric acid;

(S)-2-(4′-Amino-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(4′-Cyano-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(3′,4′-Dibromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid, sodium salt;

(S)-2-(3′-Bromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(4′-Bromo-2'-fluoro-biphenyl-4-sulfonylamino)-3-methyl-butyric acid,

(R)-2-(4′-Bromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(4′-Bromo-biphenyl-4-sulfonylamino)-propionic acid;

(S)-2-(4′-Bromo-biphenyl-4-sulfonylamino)-4-methyl-pentanoic acid;

(S)-2-(4′-Methoxy-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(4′-Fluoro-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-2-(3′-Fluoro-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

(S)-3 -Methyl-2-(4′-trifluoromethyl-biphenyl-4-sulfonylamino)-butyric acid;

2-(4′-Formyl-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

4′-(1-Carboxy-2-methyl-propylsulfamoyl)-biphenyl-4-carboxylic acid;

2-(4′-Hydroxymethyl-biphenyl-4-sulfonylamino)-3-methyl-butyric acid;

2-(4′-AminomethYl-biphenyl-4-sulfonvlamino)-3-methyl-butyric acid;

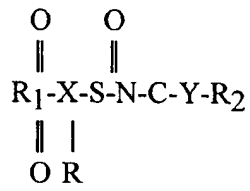
(S)-2-(4′-Bromo-biphenyl-4-sulfonylamino)-3-phenyl-propionic acid;

(S)-(4′-Isopropyl-biphenyl-4-sulfonylamino)-3-Phenyl-propionic acid;

(S)-2-(4′-bromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid; and

(S)-2-(4′-bromo-biphenyl-4-sulfonylamino)-3-methyl-butyric acid tert.-butyl ester.

18. A method according to Claim 1 utilizing a compound of the formula



I

or a pharmaceutically acceptable salt thereof wherein:

X and Y are selected from oxygen, sulfur and $(CR'R'')_n$ wherein n is an integer of from 1 to 4 and R′ and R″ are each independently hydrogen, alkyl, alkoxy, halogen, hydroxy, acyloxy, cycloalkyl, phenyl optionally substituted or R′ and R″ together form a spirocycloalkyl or a carbonyl;

R is hydrogen, a straight or branched alkyl of from 1 to 8 carbon atoms or benzyl;

R_1 and R_2 are each independently selected from

(a) phenyl or phenoxy each of which is unsubstituted or is substituted with 1 to 5 substituents selected from

phenyl,

an alkyl group having from 1 to 6 carbon atoms and which is straight or branched,

an alkoxy group having from 1 to 6 carbon atoms and which is straight or branched;

phenoxy,

hydroxy,

fluorine,

chlorine,

bromine,

nitro,

trifluoromethyl,

-COOH,

-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched,

$-(CH_2)_pNR_3R_4$ wherein p is zero or one, and each of R_3 and R_4 is selected from hydrogen or a straight or branched alkyl group having 1 to 4 carbon atoms;

(b) 1- or 2-naphthyl unsubstituted or substituted with from 1 to 3 substituents selected from

phenyl,

an alkyl group having from 1 to 6 carbon atoms and which is straight or branched,

an alkoxy group having from 1 to 6 carbon atoms and which is straight or branched;

hydroxy,

phenoxy,

fluorine,
chlorine,
bromine,
nitro,
trifluoromethyl,
-COOH,
-COOalkyl wherein alkyl has from 1 to 4 carbon atoms and is straight or branched,
-$(CH_2)_pNR_3R_4$ wherein p, R_3 and R_4 have the meanings defined above;

(c) arylalkyl;

(d) a straight or branched alkyl chain having from 1 to 20 carbon atoms and which is saturated or contains from 1 to 3 double bonds; or

(e) adamantyl or a cycloalkyl group wherein the cycloalkyl moiety has from 3 to 6 carbon atoms.

19. A compound of Claim 14 wherein R_1 is phenyl.

20. A compound of Claim 14 wherein R_1 is phenyl disubstituted in the 2,6-positions.

21. A compound of Claim 14 wherein R_2 is phenyl.

22. A compound of Claim 14 wherein R_2 is phenyl disubstituted in the 2,6-positions.

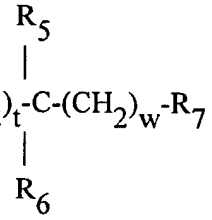
23. A compound of Claim 14 wherein each of R_1 and R_2 is phenyl.

24. A compound of Claim 16 wherein each phenyl is disubstituted in the 2,6-positions.

25. A compound of Claim 14 wherein R_1 is phenyl disubstituted in the 2,6-positions and R_2 is phenyl trisubstituted in the 2,4,6-positions.

26. A compound of Claim 14 wherein R_1 is 2,6-bis(1-methylethyl)phenyl and R_2 is 2,6-bis(1-methylethyl)phenyl or 2,4,6-tris(1-methylethyl)phenyl.

27. A compound of Claim 14 wherein R_1 is phenyl or isophenyl disubstituted in the 2,6-positions, wherein R_2 is phenyl or is phenyl disubstituted in the 2,6-positions, wherein each of R_1 and R_2 is phenyl, wherein each phenyl is disubstituted in the 2,6-position, wherein R_1 is phenyl disubstituted in the 2,6-positions and R_2 is phenyl trisubstituted in the 2,4,6-positions, wherein R_1 is 2,6-bis(1-methylethyl)phenyl and R_2 is 2,6-bis(1-methylethyl)phenyl or 2,4,6-tris(1-methylelthyl)phenyl, wherein one of R_1 and R_2 is the group



wherein t is zero or 1 to 4; w is zero or 1 to 4 with the proviso that the sum of t and w is not greater than 5; R_5 and R_6 are each independently selected from hydrogen or alkyl having from 1 to 6 carbon atoms, or when R_5 is hydrogen, R_6 can be selected from the groups defined for R_7; and R_7 is phenyl or phenyl substituted with from 1 to 3 substituents selected from a straight or branched alkyl group having from 1 to 6 carbon atoms, straight or branched alkoxy group having from 1 to 6 carbon atoms, phenoxy, hydroxy, fluorine, chlorine, bromine, nitro, trifluoromethyl, -COOH, COOalkyl wherein alkyl has from 1 to 4 carbon atoms, or $-(CH_2)_pNR_3R_4$ wherein P, R_3 and R_4 have the meanings defined above.

28. A compound according to Claim 14 wherein

X is oxygen, sulfur or $(CR'R'')_n$;

Y is oxygen, sulfur or $(CR'R'')_n$ with the proviso that at least one of X or Y is $(CR'R'')_n$ wherein n is an integer of from 1 to 4 and R′ and R″ are each independently hydrogen, straight or branched alkyl of from 1 to 6 carbons, optionally substituted phenyl, halogen, hydroxy, alkoxy, acyloxy, cycloalkyl, or R′ and R″ taken together form a carbonyl or a spirocycloalkyl group of from 3 to 10 carbons;

R is hydrogen;

R_1 is phenyl optionally substituted, straight or branched alkyl of from 1 to 10 carbon atoms, cycloalkyl of from 3 to 10 carbon atoms;

R_2 is phenyl optionally substituted, straight or branched alkyl of from 1 to 10 carbon atoms, cycloalkyl of from 3 to 8 carbon atoms, phenoxy optionally substituted.

29. A compound according to Claim 14 wherein

X is oxygen;

Y is $(CR'R'')_n$ wherein n is an integer of from 1 to 2;

R is hydrogen;

R_1 is optionally substituted phenyl;

R_2 is optionally substituted phenyl or phenoxy, straight or branched alkyl of from 1 to 10 carbons, or cycloalkyl of from 3 to 10 carbons;

R′ and R″ are each independently hydrogen, straight or branched alkyl of from 1 to 6 carbons, optionally substituted phenyl, halogen, hydroxy, alkoxy, acyloxy, cycloalkyl, or R′ and R″ taken together form a carbonyl or a spirocycloalkyl.

30. A compound according to Claim 14 sulfamic acid[[2,4,6-tris(1-methyl-ethyl)phenyl]acetyl-2,6-bis(1-methylethyl)phenyl ester.

31. A compound of Claim 14 selected from:

Sulfamic acid (phenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl-2,4,6-tris(1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,4,6-tris(1-methylethyl)phenyl ester,

Sulfamic acid[adamantaneacetyl]-2,6-bis[1-methylethyl)phenyl ester,

Sulfamic acid[[2,6-bis(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester-sodium salt,

Sulfamic acid[[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester-sodium salt,

Sulfamic acid (decanoyl)-2,6-bis-(1-methylethyl)phenyl ester,

Sulfamic acid (dodecanoyl)-2,6-bis-(1-methylethyl)phenyl ester,

2,6-Bis(1-methylethyl)-N-[[[2,4,6-tris(1-methylethyl)phenyl]-methyl]sulfonyl]benzeneacetamide,

2,6-Bis(1-methylethyl)-N-[[[2,4,6-tris(1-methylethyl)phenyl]-methyl]sulfonyl]benzeneacetamide-sodium salt,

2,6-Bis(1-methylethyl)phenyl[[[2,4,6-tris(1-methylethyl)phenyl]-methyl]sulfonyl]carbamate,

2,6-Bis(1-methylethyl)phenyl[[[2,4,6-tris(1-methylethyl)phenyl]-methyl]sulfonyl]carbamate-sodium salt,

Sulfamic acid (1-oxo-3,3-diphenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,6-dichlorophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,6-dichlorophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid trans-[(2-phenylcyclopropyl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,5-dimethoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,4,6-trimethoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2,4,6-trimethylphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-thiophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [3-thiophenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-methoxyphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (oxophenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [2-trifluoromethylphenyl(acetyl)]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2-phenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclopentylphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclohexylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (diphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (triphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(1-phenylcyclopentyl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (3-methyl-1-oxo-2-phenylpentyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2-phenylbutyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (cyclohexylphenylacetyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-2,2-diphenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(9H-fluoren-9-yl)carbonyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid (1-oxo-3-phenylpropyl)-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [1-oxo-3-[2,4,6-tris(1-methylethyl)phenyl]-2-propenyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [1-oxo-3-[2,4,6-tris(1-methylethyl)phenyl]propyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [(acetyloxy)[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [hydroxy[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

Sulfamic acid [fluoro[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

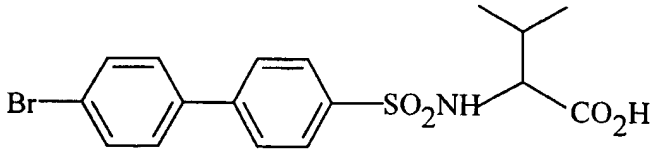
Sulfamic acid (3-methyl-1-oxo-2-phenylpentyl)-2,6-bis(1-methylethyl)phenyl ester sodium salt,

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenoxy]acetyl]-2,6-bis(1-methylethyl)phenyl ester,

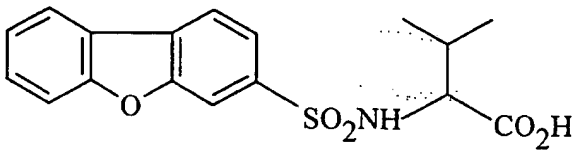
Sulfamic acid [[2,6-bis(1-methylethyl)phenoxy]acetyl]-2,6-bis-(1-methylethyl)phenyl ester, and

Sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(phenyl)phenyl ester.

32. A method according to Claim 1 wherein the MMP inhibitor is selected from



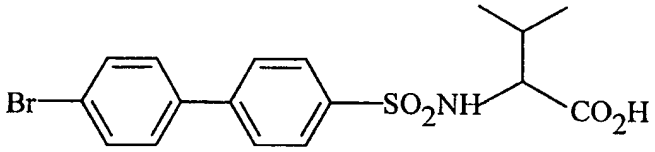
and



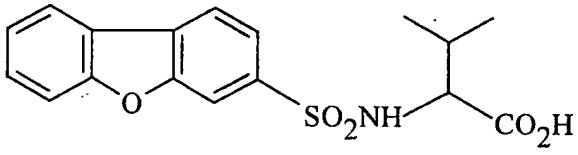
and the ACAT inhibitor is selected from [(2,4,6-triisopropyl-phenyl)-acetyl]-sulfamic acid 2,6-diisopropyl-phenyl ester and N-(2,6-diisopropyl-phenyl)-2-(2-dodecyl-2H-tetrazol-5-yl)-2-phenyl-acetamide are administered.

33. A pharmaceutical composition for treating and/or preventing atherosclerotic lesions comprising a therapeutically effective amount of an ACAT inhibitor and a MMP inhibitor.

34. A method according to Claim 1 wherein the MMP inhibitor is selected from



and



and the ACAT inhibitor is selected from [(2,4,6-triisopropyl-phenyl)-acetyl]-sulfamic acid 2,6-diisopropyl-phenyl ester and N-(2,6-diisopropyl-phenyl)-2-(2-dodecyl-2H-tetrazol-5-yl)-2-phenyl-acetamide are administered.

35. A method according to Claim 1 wherein the ACAT inhibitor is selected from:

4-Hexadecylamino-benzoic acid monosodium salt;

3,5-Dimethyl-1-[5-(1,4,5-triphenyl-2H-imidazol-2-ylsulfanyl)-pentyl]-1H-pyrazole monosodium salt;

8-(1,4,5-Triphenyl-2H-imidazol-2-yloxy)-octanoic acid;

9-Bromo-6,11-dihydro-dibenzo[b,e]oxepine-11-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

5-((3,5-Di-tert-butyl-4-hydroxy-phenylamino)-{[4-(2,2-dimethyl-propyl)-benzyl]-hexyl-amino}-methylene)-2,2-dimethyl-[1,3]dioxane-4,6-dione;

3-(2,4-Difluoro-phenyl)-1-[4-(2,2-dimethyl-propyl)-benzyl]-1-heptyl-urea;

1-Heptyl-1-[4-(3-methyl-butyl)-benzyl]-3-(2,4,6-trifluoro-phenyl)-urea;

3-(2,4-Difluoro-phenyl)-1-[5-(4,5-diphenyl-1H-imidazol-2-ylsulfanyl)-pentyl]-1-heptyl-urea;

1-Butyl-3-{2-[3-(5-ethyl-4-phenyl-imidazol-1-yl)-propoxy]-6-methyl-phenyl}-urea;

1-(2-{2-[4-(2,2-Dimethyl-propyl)-phenyl]-ethyl}-4,6-difluoro-phenyl)-3-heptyl-urea;

Octadeca-9,12-dienoic acid (1-phenyl-ethyl)-amide;

3-(1H-Indol-3-yl)-2-octadec-9-enoylamino-propionic acid ethyl ester;

3-(Dimethyl-nonyl-silanyl)-N-(1-phenyl-2-p-tolyl-ethyl)-propionamide;

(R)2-Hexyl-decanoic acid (6-methyl-2,4-bis-methylsulfanyl-pyridin-3-yl)-amide;

N-[2-(3,5-Di-tert-butyl-4-hydroxy-phenyl)-ethyl]-4-fluoro-benzenesulfonamide;

2-(2-Ethoxy-ethylsulfanyl)-4,5-diphenyl-1H-imidazole;

4-Cyano-N-[2-(4-cyano-phenyl)-3-methyl-5,5-bis-trifluoromethyl-4,5-dihydro-3H-imidazol-4-yl]-N-methyl-benzamide;

1-{3-[3-(1-Methyl-1H-imidazol-2-yl)-2-phenethyl-2H-chromen-6-yloxy]-propyl}-cyclopentanecarboxylic acid ethyl ester;

1-[4-(2-Chloro-phenyl)-2-ethyl-thieno[2,3-b]pyridin-5-yl]-3-(2,4-difluoro-phenyl)-urea;

1-(2-Cyclohexyl-[1,3]dithiolan-2-ylmethyl)-3-(2,6-diisopropyl-phenyl)-urea;

1-Cycloheptyl-1-(2,3-dihydro-benzo[1,4]dioxin-5-ylmethyl)-3-(2,4,6-trimethyl-phenyl)-urea;

1-{2-[4-(1,2-Dimethoxy-ethoxy)-phenyl]-ethyl}-3-(2,4-dimethoxy-phenyl)-1-heptyl-urea;

2-(4-{2-[3-(2,4-Dimethoxy-phenyl)-1-heptyl-ureido]-ethyl}-phenoxy)-2-methyl-propionic acid;

3-(2,4-Difluoro-phenyl)-1-octyl-1-(2,3,4,5-tetrahydro-benzo[b]oxepin-5-yl)-urea;

N-(2,6-Diisopropyl-phenyl)-2-octadecylsulfanyl-acetamide;

2-Bromo-6,11-dihydro-dibenzo[b,e]oxepine-11-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

(±)N-(1,2-Diphenyl-ethyl)-3-(2-heptyloxy-phenyl)-propionamide;

2,2-Dimethyl-dodecanoic acid (7-methoxy-4-oxo-chroman-8-yl)-amide;

(Z)1-(6,7-Dimethoxy-3,4-dihydro-1H-isoquinolin-2-yl)-octadec-9-en-1-one;

(Z)2,2,5,5-Tetramethyl-[1,3]dioxane-4-carboxylic acid [2-(2-octadec-9-enoylamino-ethylcarbamoyl)-ethyl]-amide;

1-Benzyl-1-(5-methyl-3-phenyl-benzofuran-2-ylmethyl)-3-(2,4,6-trifluoro-phenyl)-urea;

5-Chloro-3-o-tolyl-benzofuran-2-carboxylic acid (2,6-diisopropyl-phenyl)-amide;

2-(2,4a-Dimethyl-4a,5-dihydro-naphthalen-1-ylsulfanyl)-N-{2-[(6,6-dimethyl-hepta-2,4-diynyl)-pentyl-amino]-ethyl}-acetamide;

(Z)Octadec-9-enoic acid [2-(1,4-dioxa-8-aza-spiro[4.5]dec-8-yl)-1-phenyl-ethyl]-amide;

N-(4-Dihexylamino-6-mercapto-2-methyl-pyrimidin-5-yl)-4-(phenyl-propyl-amino)-butyramide;

(Z)1-(6,7-Dimethoxy-3-phenyl-3,4-dihydro-1H-isoquinolin-2-yl)-octadec-9-en-1-one;

(trans)1,4-Bis-(4-methoxy-phenyl)-3-(3-phenyl-propyl)-azetidin-2-one;

1-Butyl-3-{2-dimethylamino-6-[3-(4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-urea;

1-{2-Dimethylamino-6-[3-(4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-3-pentyl-urea;

1-{2-Dimethylamino-6-[3-(5-methyl-4-phenyl-imidazol-1-yl)-propoxy]-phenyl}-3-pentyl-urea;

1-(2-{2-[4-(2,2-Dimethyl-propyl)-phenyl]-ethyl}-4,6-difluoro-phenyl)-3-heptyl-urea;

(4S-trans)6-(4,5-Diphenyl-1H-imidazol-2-ylsulfanylmethyl)-4-hydroxy-4-methyl-tetrahydro-pyran-2-one;

2-(3-[1,3]Dioxan-2-yl-propylsulfanyl)-4,5-diphenyl-1H-imidazole;

Hydroxy-phenyl-acetic acid 3,3,5-trimethyl-cyclohexyl ester;

Acetic acid 1-(11-hydroxy-4-methoxy-9-methyl-5-oxo-5H,7H-6,12-dioxa-dibenzo[a,d]-cycloocten-3-yl)-3-methyl-butyl ester;

10-Hydroxy-2,4a,6a,6b,9,10,12a-heptamethyl-4-octadecanoyloxy-1,2,3,4,4a,5,6, 6a,6b,7,8,8a,9,10, 11,12,12a,12b,13,14b-eicosahydro-picene-2-carboxylic acid;

3-[(2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-propionic acid 2-[3-(2,2-dimethyl-propyl)-3-nonyl-ureido]-cyclohexyl ester;

1-(2,6-Diisopropyl-phenyl)-3-(2-p-tolyl-heptyl)-urea;

1-[4-(2-Chloro-phenyl)-6,8-dimethyl-quinolin-3-yl]-3-(2,4-difluoro-phenyl)-urea;

1-[4-(2-Chloro-phenyl)-1,6,7-trimethyl-2-oxo-1,2-dihydro-quinolin-3-yl]-3-(2,4-difluoro-phenyl)-urea;

1-[4-(2-Chloro-phenyl)-6,7-dimethyl-2-oxo-2H-chromen-3-yl]-3-(2,4-difluoro-phenyl)-urea;

(S)1-[6-Bromo-5-(2-chloro-phenyl)-1,3-dimethyl-2-oxo-2,3-dihydro-1H-benzo[e][1,4]-diazepin-7-yl]-3-(2-hydroxy-1-hydroxymethyl-1-methyl-ethyl)-urea;

3-(4,5-Diphenyl-1H-imidazol-2-ylsulfanylmethyl)-1-methyl-piperidine;

2-(5,5-Dimethyl-[1,3]dioxan-2-yl)-4,5-diphenyl-1H-imidazole;

2,2-Dimethyl-5-[3-(1-methyl-1H-imidazol-2-yl)-2-propyl-chroman-6-yloxy]-pentanoic acid ethyl ester;

N-(4-Hexadecylamino-benzoyl)-4-methyl-benzenesulfonamide;

2-(4-Chloro-phenyl)-6-cyclohexyl-4-(2-oxo-2-phenyl-ethyl)-6,7-dihydro-4H-1,4,6,8a-tetraaza-s-indacene-5,8-dione;

[2-(3-tert-Butyl-4-hydroxy-naphthalen-1-yl)-1-(diethoxy-phosphoryl)-vinyl]-phosphonic acid diethyl ester;

5-[1-(acetyloxy)-3-methylbutyl]-2′-(hydroxymethyl)-4-methoxy-4′-methylspiro[benzofuran-2(3H),1′-cyclohexa-2′,4′-diene]-3,6′-dione;

5-[1-(acetyloxy)-3-methylbutyl]-4-methoxy-4′-methyl-3,6-dioxospiro[benzofuran-2(3H),1′-cyclohexa-2′,4′-diene]-2′-carboxaldehyde;

(3α,4α,22α,24α)-3-hydroxy-22-[(1-oxooctadecyl)oxy]-24-norolean-12-en-29-oic acid;

1-[5-(4,5-Diphenyl-1H-imidazole-2-sulfinyl)-pentyl]-3,5-dimethyl-1H-pyrazole; and

N-butyl-3-[[(4-decyloxyphenyl)carbonyl]-amino]-4-(methylthio)-benzamide.

36. A method according to Claim 1 wherein the MMP inhibitor is selected from:

4-[2-(2-Carboxymethyl-4-phenyl-butylamino)-3-cyclohexyl propionylamino]benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butyrylamino)-3,3-methyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butyrylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-5-methyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-phenyl-butylamino)-2-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-valerylamino)-4-methyl-valerylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-phenyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino-benzoic acid methyl ester;

5-Methyl-3-(9-oxo-1,8-diaza-tricyclo[10.6.1.0 13,18]nonadeca-12(19),13,15,17-tetraen-10-ylcarbamoyl)-hexanoic acid;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-3,3-methyl-butyrylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butyrylamino)-2-cyclohexylpropionylamino]-benzoic acid methyl ester benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-valerylamino)-4-methyl-valerylamino]-benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-4-phenyl-butylamino)-3-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Methoxyaminocarbonylmethyl-4-phenyl-butylamino)-3-cyclohexylpropionylamino]benzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-5-phenyl-valerylamino)-3,3-dimethyl-butyrylamino]-benzoic acid methyl ester;

5-Methyl-3-(9-oxo-1,8-diaza-tricyclo[10.6.1.0,13,18]nonadeca-12(19),13,15,17-tetraen-10-ylcarbamoyl)-1-hexylhydroxamic acid;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino-benzoic acid methyl ester;

3-[2-(4-Methoxy-benzylsulfanyl)-2-methyl-1-phenylcarbamoyl-propylcarbamoyl]-5-methyl-hexanoic acid;

3-[2-(4-Methoxy-benzylsulfanyl)-2-methyl-1-phenylcarbamoyl-propylcarbamoyl]-5-methyl-hexanoic acid N-hydroxyamide;

4-[2-(2-Hydroxaminocarbonylmethyl-4-methyl-pentanoylamino)-2-cyclohexyl-acetylamino]-benzoic acid methyl ester;

2-(Phenyl-2-ethyl)benzoic acid N-hydroxy amide;

4-[2-(2-Acylhyrdazinomethyl-4-methyl-pentanoylamino)-3-(1H-indol-3-yl)-propionylamino]-benzoic acid methyl ester;

2-(Propylthio)-pyridine-3-N-(hydroxy)carboxamide;

4-[2-(2-Carboxymethyl-5-phenyl-pentanoylamino)-2-cyclohexylacetylamino]benzoic acid methyl ester;

[4-(N-Hydroxyamino)-2R-isobutyl-3S-((thien-2-ylthio)methyl)succinyl]-L-phenylalanine-N-methylamide;

N-Hydroxy-5-phenylpentanamide;

4-[2-(2-Carboxymethyl-5-(3-hydroxyphenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-hydroxyphenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester, trifluoroacetate salt;

2-(Phenyl-2-ethyl)pyridine-3-N-hydroxycarboxamide;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)acetyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(3-aminophenyl)acetyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-[3-(3-Hydroxy-phenyl)-propyl]-benzohydroxamic acid;

2-(Thiobenzyl)benzoic acid N-hydroxy amide;

1-(3-Phenyl-propyl)-pyrrolidine-2-hydroxamic acid;

4-[2-(2-Carboxymethyl-5-(5-hydroxyvaleroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(N'-methylureido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(triflouroacetamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-phenylacetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Hydroxaminocarbonylmethyl-2-phenylacetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-methyl-pentanoylamino)-2-cyclohexyl-acetylamino]-benzoic acid methyl ester;

2-[3-(3-Amino-phenyl)-propyl]-benzohydroxamic acid;

cis-4-Benzyloxy-pyrrolidine-2-carboxylic acid;

4-[2-(2-Carboxymethyl-5-(3-amino-4-(triflouromethyl)phenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(methanesulfamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

N-Cbz-L-Tyrosine;

N-Boc-L-Tryptophan;

4-[2-(Carboxy-2-o-tolyl-propionylamino-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-[2-(Carboxymethyl-hepanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-n-butylphenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-n-butylphenyl)-4-pentenoyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-(2-thienyl)acetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-(3-aminophenyl)-butyryl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(biphen-4-yl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

cis-4-Benzylsulfanyl-pyrrolidine-2-carboxylic acid;

2-Cyclohexylmethyl sulfonyl-benzoic acid;

Pyrrolidine-1-carbothioic acid phenethyl-amide;

3-(2-Methyl-thiazol-4-yl)-N-phenethyl-propionamide;

N-Phenyl-3-[1-(2-trimethylsilanyl-ethoxymethyl)-1H-imidazol-4-yl]-propionamide;

3-(3H-Imidazol-4-yl)-N-phenethyl-propionamide;

4-[2-(2-Carboxymethyl-5-(formamido)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-Cyclohexylmethyl sulfonyl-benzohydroxamic acid;

[2-Oxo-3-(3-phenyl-propyl)-tetrahydro-furan-3-yl]-acetic acid;

4-[2-(2-Carboxymethyl-5-(fluoren-2-yl)valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Carboxymethyl-2-(3-thienyl)acetylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

4-[2-(2-Benzylthio-3-carboxy-propionylamino)-4-methylpentanoylamino]-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-4-(2-indolyl)butyrylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

1-Allyl-3-(2-hydroxyethyl)-2-thiourea;

3-(1-Hydroxyimino-propyl)-6-phenyl-hexanoic acid;

2-(3H-Imidazol-4-ylmethyl)-N^1,N^4-diphenethyl-succinamide;

3-(2-Hydroxymethyl-3H-imidazol-4-yl)-N-phenethyl-propionamide;

6-Phenyl-3-propionyl-hexanoic acid;

4-{2-([2-Hydroxyamino-2-hydroxyimino-ethyl]-5-phenyl-pentanoylamino)-4-methyl-pentanoylamino}-benzoic acid methyl ester;

4-[2-(2-(2-Phenylcyclopropyl)succinylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid trifluoroacetate salt;

3-[1-(5,6-Dichloro-1H-benzoimidazol-2-yl)-3-methyl-butylcarbamoyl]-5-methyl-hexanoic acid;

6-Biphenyl-4-yl-3-[1-(5,6-dichloro-1H-benzoimidazol-2-yl)-3-methyl-butylcarbamoyl]-5-methyl-hexanoic acid;

2-Carboxymethyl-heptanoyl-2-(N-methylcarboxamide)piperidine;

4-[2-(2-(2-Phenylcyclopropyl)succinylamino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

2-Carboxymethyl-heptanoyl-3-(N-methylcarboxamide)-hexahydropyridazine;

6-Biphenyl-4-yl-3-[1-[3-(3-hydroxy-ethyl)-phenylcarbamoyl]-2,2-dimethyl-propylcarbamoyl]-hexanoic acid;

2R-(3-(4-Biphenyl)propyl-N-(2R-hydroxy-3-(2-hydroxyphenyl)-5-methyl-3S-hexyl)succinamide;

6-Biphenyl-4-yl-3-[1-[3-(2-aminoethyl)-phenylcarbamoyl]-2,2-dimethyl-propylcarbamoyl]-hexanoic acid;

2R-(3-(4-Biphenyl)propyl)-N-(diphenylmethyl)succinamide;

2R-(3-(4-Biphenyl)propyl)-N-(phenylmethyl)succinamide;

2-(2-Oxo-imidazolidin-4-ylmethyl)-5-phenyl-pentanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N^1-[1-(5,6-dichloro-1H-benzoimidazol-2-yl)-3-methyl-butyl]-N^4-hydroxy-succinamide hexanoic acid;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid, N-hydroxyamide;

2R-(3-(4-Biphenyl)propyl)-N-((1-hydroxy-1-methylethyl)phenylmethyl)succinamide;

6-Biphenyl-4-yl-3-[1-phenylcarbamoyl-2-(4-cyano-benzylsulfanyl)-2-methyl-propylcarbamoyl]-hexanoic acid;

4-{2-[2-Carboxymethyl-5-(4'-hydroxy-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

1-(N-Methyl-N-phenethylthiocarbomyl)-pyrrolidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-({cyclohexyl-[2-(4-sulfanoyl-phenyl)-ethylcarbamoyl]-methyl}-carbamoyl)-hexanoic acid;

3R(6-(4-Biphenyl)-3-(N-benzylcarbamoyl))-hexanoic acid N-hydroxyamide;

[3-(3-Biphenyl-4-yl-propyl)-2-oxo-pyrrolidin-3-yl]-acetic acid;

2-Benzylsulfonyl-cyclopent-1-ene-carboxylic acid hydroxamide;

[2-Oxo-3-(3-phenyl-propyl)-pyrrolidin-3-yl]-acetic acid;

[3-(3-Naphthalen-2-yl-propyl)-2-oxo-pyrrolidin-3-yl]-acetic acid;

2-Benzylsulfonyl-cyclohex-1-enecarboxylic acid hydroxy amide;

6-Benzylsulfonyl-cyclohex-1-enecarboxylic acid hydroxy amide;

2R-(3-(4-Biphenyl)propyl)-N-(3-methylpyridine)succinamide;

{3-[3-(3-Hydroxy-phenyl)-propyl]-2-oxo-pyrrolidin-3-yl}-acetic acid;

6-Biphenyl-4-yl-{[cyclohexyl-(3-morpholin-4-yl-propylcarbamoyl)-methyl]-carbamoyl}hexanoic acid;

[2-Oxo-3-(3-biphenyl-propyl)-tetrahydro-furan-3-yl]-acetic acid;

4-[2-(2-Thioamidomethyl-5-phenyl-valerylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

4-[2-(2-Amino-2-hydroxyimino-ethyl-5-phenyl-valerylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfamoyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(2-hydroxyethylsulfamoyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

1-(N-Hydroxy)-3-(2-bibenzyl)urea;

4-(2-{5-[7-(2-Amino-acetylamino)-9H-fluoren-2-yl]-2-carboxymethyl-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester TFA salt;

3R-(6-(4-Biphenyl)propyl)-N-(3-methylpyridinecarbamoyl)-hexanoic acid N-hydroxy amide;

6-Biphenyl-4-yl-3-[cyclohexyl-(4-(2-hydroxy-ethylsulfamoyl)-phenylcarbamoyl)-methylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[cyclohexyl-(4-(2-dimethylamino-ethylsulfamoyl)-phenylcarbamoyl)-methylcarbamoyl]-hexanoic acid, trifluoroacetate salt;

4-(2-{2-Carboxymethyl-5-[4-(1H-tetrazol-5-yl)-phenyl]-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester;

4-[2-(2-Carboxymethyl-5-(4-(2-hydroxy-ethyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

4-(2-{[5-Hydroxyamino-3-(3-phenyl-propyl)-3,4-dihydro-2-H-pyrrole-3-carbonyl]-amino}-4-methyl-pentanoylamino)benzoic acid methyl ester;

5-Hydroxyamino-3-(3-phenyl-propyl)-3,4-dihydro-2-H-pyrrole-3-carboxylic acid(2-cyclohexyl-1-methylcarbamoyl-ethyl)amide;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-(3-morpholin-4-yl-sulfamoyl)-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfanyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfonyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(5-Biphenyl-4-yl-2-carboxymethyl-pentanoylamino)-pent-4-enoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-(2-{[5-Hydroxyamino-3-(3-pentyl)-3,4-dihydro-2-H-pyrrole-3-carbonyl]-amino}-4-methyl-pentanoylamino)benzoic acid methyl ester;

5-Hydroxyamino-3-(3-pentyl)-3,4-dihydro-2-H-pyrrole-3-carboxylic acid(2-cyclohexyl-1-methylcarbamoyl-ethyl)amide;

6-Biphenyl-4-yl-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-cyano-biphenyl-4-yl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-y-3-(R)-(2-hydroxy-1-(S)-phenyl-ethylcarbamoyl)-hexanoic acid;

3-(R)-(1-(R)-Benzyl-2-hydroxy-ethylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-hydroxymethyl-ethylcarbomyl)-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-pyridin-4-yl-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]benzoic acid methyl ester;

6-Biphenyl-4-yl(2-hydroxy-2-methyl-1-phenylcarbamoyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl(2-hydroxy-2-methyl-1-phenylcarbamoyl-propylcarbamoyl)-hexanoic acid;

3-{2-Allylsufamyl-2-methyl-1-[2-(4-sulfamoyl-phenyl)-ethylcarbamoyl]-propylcarbamoyl}-6-biphenyl-4-yl-hexanoic acid;

4-[2-(5-Biphenyl-4yl-2-carboxymethyl-pentanoylamino)-4,5-dihydroxy-pentanoylamino]-benzoic acid methyl ester;

4-(2-{5-[4'-(2-Amino-ethoxy)-biphenyl-4-yl]-2-carboxymethyl-pentanoylamino}-4-methyl-pentanoylamino)-benzoic acid methyl ester;

6-Biphenyl-4-y-3-(R)-(2-hydroxy-1-(S)-phenyl-ethylcarbamoyl)-hexanehydroxamic acid;

3-(R)-(1-(R)-Benzyl-2-hydroxy-ethylcarbamoyl)-6-biphenyl-4-yl-hexanehydroxamic acid;

N-[5-(Biphenyl-4-yl)-2-(N-hydroxyformamido)methylpentanoyl]-tert-leucine, N-(pyrid-4-yl)amide;

[3-(3-Naphthalen-2-yl-propyl)-2-oxo-tetrahydro-furan-3-yl]-acetic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-hydroxymethyl-ethylcarbomyl)-hexanehydroxamic acid;

4-[2-(2-Carboxymethyl-5-naphthalen-2-yl-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

3-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-5-methyl-hexanoicacid;

N1-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propyl]-N4-hydroxy-2-isobutyl-succinamide;

4-{2-[2-Carboxymethyl-5-(2-fluoro-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

6-Biphenyl-4-yl-3(R)-(1(S)-hyroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic acid;

4-{2-[5-Biphen-4-yl-2-(1-carboxy-ethylamino)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

6-Biphenyl-4-yl-3(R)-(1(S)-hyroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanehydroxamic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

2-(Biphenyl-4-ylsulfonyl)-cyclohex-1-enecarboxylic acid hydroxyamide;

6-(Biphenyl-4-ylsulfonyl)-cyclohex-1-enecarboxylic acid hydroxyamide;

2-Phenethylsulfanyl-cyclohex-1-enecarboxylic acid hydroxyamide;

6-(4′-cyano-biphenyl-4-yl)-3-[2-hydroxy-1-(4-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylcarbamoyl}-pyrrolidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(4S-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

4-[2-(2-Carboxymethyl-5-(4-(2-hydroxy-3,3,3-trifluoropropyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

2-Benzylsulfanyl-cyclohexancarboxylic acid hydroxamide;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylcarbamoyl}-pyrrolidine-2-carboxylic acid;

trans-2-Benzylsulfanyl-cyclohexancarboxylic acid hydroxamide;

4-[2-(2-Carboxymethyl-5-(4-(2-methylthiazol-4-yl)phenyl)-valeroyl)amino)-4-methyl-valeroyl]aminobenzoic acid methyl ester;

1-{1-[1-(4-Methoxycarbonyl-phenylcarbamoyl)-3-methyl-butylcarbamoyl]-3-methyl-butylthiocarbamoyl}-pyrrolidine-2-carboxylic acid;

3-[(Cyclohexyl-(4-(2-hydroxy-ethylsulfamoyl)-phenylcarbamoyl)-methyl)-carbamoyl]-6-(4-pyridin-4-yl-phenyl)-hexanoic acid trifluoroacetate salt;

trans-2-(Biphenyl-4-yl-methylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2,2-dimethyl-but-3-enylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2,2-dimethyl-but-3-enylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanoic acid;

3-(R)-(2-(R)-Benzyloxy-1-(S)-hydroxymethyl-propylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

4-[4-Methyl-2-(2-nitromethyl-5-phenyl-pentanoylamino)-pentanoylamino]-benzoic acid methyl ester;

6-Biphenyl-4-yl-3-[3-methyl-1-(4-(2-hydroxyethylsulfamoyl)-phenylcarbamoyl)-butylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxymethyl-2-phenyl-ethylcarbamoyl)-hexanoic acid;

N^1-(1-Benzyl-2-hydroxy-ethyl)-2-(3-biphenyl-4-yl-propyl)-N^4-hydroxy-succinamide;

6-Biphenyl-4-yl-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanehydroxamic acid;

N-Hydroxy-2-[2-Oxo-3-(3-phenyl-propyl)-tetrahydro-furan-3-yl]-acetamide;

4-[2-(2-Carboxymethyl-5-(2-hydroxy-biphen-4-yl)-valeroylamino)-4-methyl-valeroylamino]-benzoic acid methyl ester;

N^1-(2-Benzyloxy-1-hydroxymethyl-propyl)-2-(3-biphenyl-4-yl-propyl)-N^4-hydroxy-succinamide;

trans-2-(4-Phenoxy-benzylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

2-(4-Indol-1-yl-benzylsulfanyl)-cyclohexancarboxylic acid hydroxamide;

6-Biphenyl-4-yl-3-[2-hydroxy-2-methyl-1-(4S-methylsulfinyl-phenylcarbamoyl)-propylcarbamoyl]-hexanoic acid;

6-Biphenyl-4-yl-3-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-ylcarbamoyl)-hexanoic acid;

5-Biphenyl-4-yl-2-[(formyl-hydroxy-amino)-methyl]-pentanoic acid{1-[4-(2-dimethylamino-ethylsulfamoyl)-phenylcarbamoyl]-3-methyl-butyl}-amide;

2-(3-Biphenyl-4-yl-propyl)-N^4-hydroxy-N1-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-yl)-succinamide;

6-Biphenyl-4-yl-3-(2,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-3-ylcarbamoyl)-hexanoic acid;

N-[2,2-Dimethyl-1S-(pyridin-4-ylcarbamoyl)-propyl]-3R-thiophen-3-yl-succinamic acid;

4-[2S-(2R-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxy-propionylamido)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

3-(R)-(2-Benzyloxy-phenyl)-1-(S)-hydroxymethyl-ethylcarbamoyl)-6-biphenyl-4-yl-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-(S)-(4-hydroxy-benzyl)-ethylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(1-hydroxyimino-ethyl)-hexanoic acid;

N-[2-(3-(4-biphenyl)propyl)-5,5-difluoro-4-oxopentanoyl)-L-t-leucine, N′-4-(methylthio)phenyl amide;

6-Biphenyl-4-yl-3-(R)-(2-hydroxy-1-(S)-(4-hydroxy-benzyl)-ethylcarbamoyl)-hexanehydroxamic acid;

4-{2-[2-carboxymethyl-5-(4′-sulfamoyl-biphenyl-4-yl)-pentanoylamino]-4-methyl-pentanoylamino}-benzoic acid methyl ester;

2-(2-Biphenyl-4-yl-ethylsulfanyl)-cyclohexane carboxylic acid hydroxyamide;

3-Acetyl-6-biphenyl-4-yl-3-hexanoic acid;

N-[5-(Biphen-4-yl)-2-(1-carboxy-2-hydroxybut-1-yl)pentanoyl]-t-L-leucine, N′-(4-methylthiophenyl)amide;

6-Biphenyl-4-yl-3-(2-Hydroxy-cyclohexylcarbamoyl)-hexanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N4-hydroxy-N1-(2-hydroxy-cyclohexyl)-succinamide;

6-Biphenyl-4-yl-3-(1-hydroxyimino-ethyl)-hexanoic acid hydroxamide;

6-Biphenyl-4-yl-3-(2-Hydroxy-cyclohexylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-[2,2-dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-hexanoic acid ethyl ester;

2-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxy-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

N-[5-(Biphen-4-yl)-2-(1-carboxy-2-hydroxyethyl)pentanoyl]-L-t-leucine, N′-(4-methylthiophenyl)amide;

3-(R)-(2-Hydroxy-1-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-6-(4-(2-methyl-thiazol-4-yl)-phenyl)-hexanoic acid;

3-(R)-(2-Hydroxy-1-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-6-(4-(2-methyl-thiazol-4-yl)-phenyl)-hexanehydroxamic acid;

5-Biphenyl-4-yl-2-(1-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-pentanoic acid;

2-(3-Biphenyl-4-yl-propyl)-N-hydroxy-N′-(1-hydroxymethyl-3-methylsulfanyl-propyl)malonamide;

6-Biphenyl-4-yl-3-(3-hydroxy-piperidine-1-carbonyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(3-hydroxy-piperidine-1-carbonyl)-hexanoic acid-hydroxyamide;

1-(4-Methoxy-benzenesulfonyl)-piperidine-2-carboxylic acid hydroxamide;

1-[4-Bromo-phenoxy)-benzenesulfonyl)-piperidine-2-carboxylic acidhydroxyamide;

N-(1-Benzyl-2-methoxy-ethyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamic acid;

N-(1-Benzyl-2-methoxy-ethyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamichydroxamic acid;

6-Biphenyl-4-yl-3(R)-2(S)-hydroxy-(1(S)-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic acid;

3-(1-Benzyl-2-hydroxy-ethylcarbamoyl)-5-methyl-hexanoic acid;

N^1-(1-benzyl-2-hydroxy-ethyl)-N^4-hydroxy-2-isobutyl-succinamide;

6-Biphenyl-4-yl-3(R)-2(S)-hydroxy-(1(S)-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-hexanoic hydroxamic acid;

1-[4-Bromo-phenoxy)-benzenesulfonyl)-piperidine-2-carboxylic acid;

6-Biphenyl-4-yl-3-(2-hydroxy-1-hydroxmethyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-cyclohexyl-1-(S)-carbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(2-hydroxy-1-hydroxmethyl-propylcarbamoyl)-hexanoichydroxamic acid;

2S-[(1S-Benzyl-2-hydroxyethylcarbamoyl)-3R-biphenyl-4-yl-pyrrol-1-yl-methyl]-pentanoic acid;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-(2R-hydroxy-cyclohexyl-1R-yl)-succinamic acid;

2-(3-Biphenyl-4-yl-pyrrol-1-yl)-3-carboxamate-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

trans-2-(3-Biphenyl-4-yl-propyl)-cyclohexane carboxylic acid;

trans-2-(3-Biphenyl-4-yl-propyl)-cyclohexane carboxylic acid hydroxyamide;

6-Biphenyl-4-yl-3-(R)-(1-(S)-hydroxymethyl-2-(3-pyridyl)-ethylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-2-(S)-hydroxy-3-(R)-(1-hydroxymethyl-2-(S)-(1H-imidazol-4-yl)-ethylcarbamoyl)-hexanoic acid;

1-[4-Biphenyl-4-yloxy)-benzenesulfonyl)-piperidine-2-carboxylic acid;

1-[4-Biphenyl-4-yloxy)-benzenesulfonyl)-piperidine-2-carboxylic acidhydroxamide;

1-(4-Phenoxy-benzenesulfonyl)-piperidine-2-carboxylic acidhydroxamide;

6-Biphenyl-4-yl-2S-hydroxy-3R-(1S-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-hexanoic acid;

6-Biphenyl-4-yl-3-(R)-(1-(S)-hydroxymethyl-2-(3-pyridyl)-ethylcarbamoyl)-hexanehydroxamic acid;

6-Biphenyl-4-yl-2S-hydroxy-3R-(1S-hydroxymethyl-3-methylsulfanyl-propylcarbamoyl)-hexanoic hydroxmic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-4-(tert-butoxycarbonyl)-piperazine-2-carboxylic acidhydroxyamide;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-piperazine-2-carboxylic acidhydroxyamide;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[2-hydroxy-1S-(1H-imidazol-4-yl-methyl)-ethyl]-succinamic acid trifluoroacetate;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[1S-(methoxy-methylcarbamoyl)-3-methyl-butyl]-succinamic acid;

N-(1-Acetyl-3-methyl-butyl)-3-(3-biphenyl-4-yl-pyrrol-1-yl)-succinamic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-1-tetrahydrofuran-3-(S)-ylcarbamoyl)-hexanoic acid;

3-[2,2-Dimethyl-1-(pyridin-4-ylcarbamoyl)-propylcarbamoyl]-2-hydroxy-5-methyl-hexanoic acid-hydrochloride salt;

N^4-(2,2-Dimethyl-1-methylcarbamoyl-propyl)-2, N^1-dihydroxy-3-isobutyl-succinamide;

6-Biphenyl-4-yl-3-(R)-(2-oxo-azepan-3-(S)-ylcarbamoyl)-hexanoic acid;

N-(1-Benzyl-2-hydroxy-ethyl)-3-(4-biphenyl-4-yl-pyrazol-1-yl)-succinamic acid;

N-(8-Oxo-4-oxa-1,7-diaza-tricyclo[9.6.1.0 12,17]octadeca-11(18),12(17),13,15-tetraen-9R-yl)-3S-(3-phenyl-pyrrol-1-yl)-succinamic acid;

4-Acetyl-1-[4-phenoxy-benzenesulfonyl]-piperazine-2-carboxylic acid, N-hydroxyamide;

1-(Diphenylphosphinic)-piperidine-2-carboxylic acid hydroxamide;

3R-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-[3S-(2RS-hydroxy-5-methyl)-hexyl]-succinamic acid;

N-(1-(S)-Benzyl-2-hydroxy-ethyl)-3-(R)-(2-biphenyl-4-yl-cyclopropylmethyl)-succinamic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-1-tetrahydrofuran-3-(S)-ylcarbamoyl)-hexanehydroxamic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-4-methyl-piperazine-2-carboxylic acid N-hydroxyamide;

4-(4-Methoxy-benzenesulfonyl)-thiomorpholine-3-carboxylic acidhydroxyamide;

3-(Diphenylphosphinic)-propanoic acid;

3-(Diphenylphosphinic)-propanoic acid hydroxyamide;

4-[2-(2-Carboxymethyl-5-(4-(3-hydroxy-propyl)-phenyl)-pentanoylamino)-4-methyl-pentanoylamino]-benzoic acid methyl ester;

1-[4-(4-Chlorophenoxy)benzenesulfonyl]-N-hydroxy-4-(N-methylcarbamoyl)piperazine-2-carboxamide;

4-[4-(4-Bromo-phenoxy)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid N-hydroxyamide;

3-(3-Biphenyl-4-yl-pyrrol-1-yl)-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

1-[4-Phenoxy-benzenesulfonyl]-piperazine-2-carboxylic acid, N-hydroxyamide;

4[4-Phenoxy-benzenesulfonyl]-thiomorpholine-3-carboxylic acid N-hydroxyamide;

3-[2-Biphenyl-4-yl-ethylsulfanyl]-tetrahydro-pyran--4-carboxylic acid N-hydroxyamide;

6-Biphenyl-4-yl-3-(carboxylic acid)-hexanoic acid;

1-[4-(4-Bromo-phenoxy)-benzenesulfonyl]piperdine-2-amidoxime;

2-(3-Biphenylnitrile-4-yl-pyrrol-1-yl)-3-carboxy-N-(1-hydroxy-3-phenyl-prop-2-yl)-propionamide;

{3-[3-(3-Amino-phenyl)-propyl]-2-oxo-tetrahydro-furan-3-yl}-acetic acid;

6-Biphenyl-4-yl-2S-hydroxy-3R-(carboxylic acid)-hexanoic acid;

5-Biphenylvaleric acid;

1-[4-(Methoxy)-benzenesulfonyl]piperdine-2-amidoxime;

1-[4-Phenoxy-benzenesulfonyl]-4-methyl-piperazine-2-carboxylic acid N-hydroxyamide;

{3-(3-(3-Methylamino-phenyl)-propyl)-2-oxo-tetrahydro-furan-3-yl}-acetic acid;

6-Biphenyl-4-yl-3-(R)-(2-oxo-azepan-3-(S)-ylcarbamoyl)-hexanehydroxamic acid;

4-(1H-Indole-2-sulfonyl)-thiomorpholine-3-carboxylic acid hydroxyamide;

1R-[4-Bromo-phenoxy)-benzenesulfonyl)-N-amino-piperidine-2-carboxamide;

2-(3-Biphenyl-4-yl-propyl)-3, N-4-dihydroxy-N^1-(1(S)-hydroxymethyl-3-methanesulfinyl-propyl)-succinamide;

N-(1-Benzyl-2-hydroxy-ethyl)-3-[3-(4′-carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-succinamic acid;

1-(Methyl-phenylphosphinic)-piperidine-2-(R)-carboxylic acid hydroxamide;

4-(4-(4-Chlorophenoxy)benzenesulfonyl)-N-hydroxy-morpholine-3R-carboxamide;

2S-[1R-(3-(4′-Cyano-biphenyl-4-yl)-pyrrol-1-yl)-N-(2,2-dimethyl-1S-hydroxymethylpropylcarbamoyl)-methyl)]-pentanoic acid;

2(S,R)-{1S-Benzyl-2-hydroxyethylcarbamoyl-[3R-(4'-cyano-biphenyl-4-yl)-pyrrol-1-yl]-methyl}pentanoic acid;

2S-[3-(Biphenyl-4-yl)-pyrrol-1R-yl-(1S-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-methyl]-5-hydroxypentanoic acid;

1-(1,3-Dihydro-isoindole-2-sulfonyl)-piperidine-2-carboxylic acid hydroxamide;

3-[3-(4'-Carbamoyl-biphenyl-4-yl]-pyrrol-1-yl)-N-(1-hydroxymethyl-2,2-dimethyl-propyl)-succinamic acid;

4-Methyl-1-(4-(4-chlorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochloride;

1-[4-Chlorophenoxybenzenesulfonyl]-N-hydroxy-2R-piperazinecarboxamide;

2-(3-Phenyl-propylsulfonyl)-cyclohexane carboxylic acid hydroxamide;

1-(Pyrolidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1-(Piperidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

4-[4-Bromo-phenoxy-benzenesulfonyl]-oxothiomorpholine-3-carboxylic acid-N-hydroxyamide;

1-[4-(4-Methoxy-phenylsulfanyl)-benzenesulfonyl]-piperdine-2-carboxylic acid hydroxyamide;

1-[4-(4-Nitrile-phenoxy)-benzenesulfonyl]-4-(tert-butoxycarbonyl)-piperazine-2-carboxylic acid N-hydroxyamide;

2S-[3-(Biphenyl-4-yl)-pyrrol-1R-yl-(1S-hydroxymethyl-2,2-dimethyl-propylcarbamoyl)-methyl]-pent-4-enoic acid;

6-Oxo-3-(4-phenoxy-benzenesulfonyl)-hexahydro-pyrimidine-4-carboxylic acid hydroxamate;

4-(t-Butoxycabonyl)-1-(4-(pyridin-2-yl)oxybenzensulfonyl)-N-hydroxy-piperazine-2-carboxamide;

4-[(4-Fluorophenoxy)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid-N-hydroxyamide;

4-[4-(Fluoro-phenoxy)-benzenesulfonyl]-oxothiomorpholine-3-carboxylic acid-N-hydroxyamide;

N-(2,2-Dimethyl-1S-hydroxymethyl-propyl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(1S-Benzyl-2-hydroxy-ethyl)-3S-(5-biphenyl-4-yl-furan-2-yl)-succinamic acid;

4-(4-Butoxy-benzenesulfonyl)-thiomorpholine-3-carboxylic acid hydroxyamide;

4-(4-Butoxy-benzenesulfonyl)-1-oxothiomorpholine-3-carboxylic acid hydroxyamide;

1-[4-(4-Fluorophenyl)benzenesulfonyl]-4-(tert-butoxycarboxyl)-2R-piperazine-2-carboxylic acid hydroxyamide;

1-((4-(4-Chlorophenyl)-piperazine)-1-sulfonyl)-piperidine-2-carboxylic acid hydroxamide;

cis-2-Phenethylsulfanyl-cyclohexanecarboxylic acid hydroxyamide;

N-(2-Hydroxy-1S-phenyl-ethyl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

1-[4-(4-Fluorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochoride;

1-(Diphenylphosphinic)-pyrolidine-2-(R)-carboxylic acid-hydroxyamide;

N,N-{(Diphenylphosphinic)-(acetic acid-sodium salt)}-hydrazide;

N-(1-Benzyl-2-hydroxy-ethyl)-3-(1-biphenyl-4-yl-1H-pyrrol-3-yl)-succinamic acid;

trans-2-Phenethylsulfonyl-cyclohexanecarboxylic acid hydroxyamide;

1-[4-(4-Flourophenyl)-piperazine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

1-[4-(4-Fluorophenylsulfanyl)-benzenesulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

4-[4-(Bromo-phenoxy)-benzenesulfonyl]-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-(3-phenyl-pyrrol-1-yl)-succinamic acid;

3R-(3-Biphenyl-4-yl)-N-(2-hydroxy-1S-hydroxymethyl-2-methyl-propyl)-succinamic acid;

1-(Pyrrolidine-1-carbonyl)-pyrrolidine-2(R)-carboxylic acid;

1-(Pyrrolidine-1-carbonyl)-pyrrolidine-2(R)-carboxylic acid hyroxyamide;

1-Phenethylcarbamoyl-pyrrolidine-2(R)-carboxylic acid;

R-4-[4-(Bromophenoxy)-benzenesulfonyl]-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

4-(Ethoxycarbonyl)methyl-1-(4-(4-chlorophenyl)benzenesulfonyl)-N-hydroxy-2R-piperazinecarboxamide hydrochloride;

N-(2R-Hydroxy-indan-1R-yl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(4,4-Dimethyl-2-oxo-tetrahydro-furan-3S-yl)-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-[3-(4-pyridin-4-yl-phenyl-4-yl)-pyrrol-1-yl]-succinamic acid;

1-Phenethylcarbamoyl-pyrrolidine-2-(R)-carboxylic acid hydroxyamide;

N-(2,2-Dimethyl-1S-methyl carbamoyl-propyl)-3R-[3-(4-propyl-phenyl)-pyrrol-1-yl]-succinamic acid;

1-(4-Benzyl-piperazine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

3(S)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

2(R)-4-Methyl-1-(4-(4-fluorophenyl)benzenesulfonyl)-N-hydroxy-piperazine-2-carboxamide;

N-(2,2-Dimethyl-1-methylcarbamoyl-propyl)-3-(5-biphenyl-4-yl-furan-2-yl)-succinamic acid;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-(3-pyridin-4-yl-pyrrol-1-yl)-succinamic acid;

1-((2-Pyridyl)-4-piperazine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

1-[4-(Pyridin-4-ylsulfamyl)-benzenesulfonyl]-piperdine-2-carboxylic acid hydroxyamide;

N-(4-Phenoxy-benzenesulfonyl)-D-tert-leucine;

N-(4-Phenoxy-benzenesulfonyl)-D-tert-leucine,N-hydroxyamide;

N-(8-oxo-4-oxa-1,7-tricyclo[9.6.1.0,12,17]octadeca-11(18),12(17),13,15-tetraen-9-yl)-3-[4-(4-pyridyl)-3-phenyl-pyrrol-1-yl)-succinamic acid;

3-[3-(4-Pyridyl)phenyl-4-yl-pyrrol-1-yl]-N-[2,2-dimethyl-1-(4-pyridyl)carbamoyl-propyl]-succinamic acid;

2,2-Dimethyl-4-[4-(pyridin-2-yloxy)-benzenesulfonyl]-thio-morpholine-3-carboxylic acid hydroxyamide;

N-[4-(4-Fluorophenoxyl)benzenesulfonyl)-D-tert-leucine;

N-[4-(4-Fluorophenoxyl)benzenesulfonyl)-D-tert-leucine, N-hydroxyamide;

2-[2-(N′-Acetyl-hydrazino)-2-oxo-ethyl]-5-biphenyl-4-yl-pentanoic acid;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide hydrochloride;

2-[4-(4-Chloro-phenoxy)-benzenesulfonylamino]-3,3-dimethyl-butyric acid;

2-[4-(4-Chloro-phenoxy)-benzenesulfonylamino)-N-hydroxy-3,3-dimethyl-butyramide;

3(R)-N-Hydroxy-4-(4-(fur-3-yl)phenoxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine, N-hydroxyamide;

2-[4-(Pyridin-2-yl-oxy)-benzenesulfonylamino]-3,3-dimethyl butyric acid;

2-[4-(Pyridin-2-yl-oxy)-benzenesulfonylamino]-N-hydroxy-3,3-dimethyl butyramide;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine;

3-[3-(4′-Carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

3-[3-(4′-Cyano-biphenyl-4-yl)-pyrrol-1-y]-N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-succinamic acid;

2-(2-Biphenyl-4-yl-ethylsulfonyl)-cyclohex-1-ene-carboxylic acid hydroxyamide;

6-(2-Biphenyl-4-yl-ethyl sufonyl)-cyclohex-1-ene-carboxylic acid hydroxyamide;

N-(4-Pyridin-4-yl-oxy-benzenesulfonyl)-3,3-dimethyl-S-(benzylthio)-D-cysteine;

3-[3-4′-Carbamoyl-biphenyl-4-yl)-pyrrol-1-yl]-N-[2,2-dimethyl-1-(pyridin-4-yl-carbamoyl)-propyl]-succinamic acid;

N-(4-Phenoxy-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine, N-hydroxyamide;

1-(4-Phenoxy-piperdine-1-sulfonyl)-piperdine-2-carboxylic acid hydroxyamide;

3(R)-4-[4-(4-Bromo)phenoxybenzenesulfonyl]-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxylic acid;

N-(4-[4-Chloro-phenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine;

N-(4-[4-Chlorophenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylthio)-D-cysteine, N-hydroxyamide;

N-(4-[4-Chlorophenoxy]-benzenesulfonyl)-3,3-dimethyl-S-(methylsulfoxy)-D-cysteine, N-hydroxyamide;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-2-ylsulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-3-ylsulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridin-4-ylsulfanyl)-butyric acid;

cis-2-(2-Phenyl-ethanesulfonyl)-cycloheaxanecarboxylic acid hydroxyamide;

3(R)-N-Hydroxy-4-(4-(imidaz-1-yl)phenoxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

4-[2-(2-Hydroxycabamoylmethyl-5-phenyl-pentanoylamino)-4-methyl-pentanoyl-benzoic acid methyl ester;

trans-2-(2-Phenyl-ethanesulfonyl)-cyclohexanecarboxylic acid hydroxyamide;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfanylmethyl)-butyric acid;

2-[4-(4-Chlorophenyl)-piperazine-1-sulfonylamino]-3-methyl-3-(pyridin-2-ylmethylsulfanyl)-butyric acid;

3R-[3-(4′-Cyano-biphenyl-4-yl)pyrrol-1-yl]-N-[2,2-dimethyl-1S-(pyridin-4-ylcarbamoyl)-propyl]-succinamic acid;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfanylmethyl)-butyric acid, N-hydroxyamide;

N-(2,2-dimethyl-1-methylcarbamoyl-propyl)-3-[1-(4-fluorophenyl)-1H-pyrrol-3-yl]-succinamic acid;

2(R)-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-ylsulfanyl)-butyric acid;

2-(2-Biphenyl-4-yl-ethanesulfonyl)-cyclohexanecarboxylic acid hydroxamate;

2-[4-(4-Chlorophenyl)-piperazine-1-sulfonylamino]-3-methyl-3-(pyridin-2ylmethylsulfanyl)-butyric acid, N-hydroxyamide;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfonylmethyl)-butyric acid;

3,3-Dimethyl-2-(4-phenoxy-phenylsulfonylmethyl)-butyric acid, N-hydroxyamide;

3-tert-Butoxycarbonylmethylsulfanyl-2-(4-(4-fluoro-phenoxy)benzenesulfonylamino)-3-methyl-butyric acid;

1-(4-Phenylsulfanyl-piperidine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1-[4-(4-Fluoro-phenoxy)-benzenesulfonyl]-3,3-dimethyl-5-oxo-piperazine-2-carboxylic acid;

N-(4-[4-Fluorophenoxy]-benzenesulfonylamino)-3-methyl-3-(1-benzyl-imidazole-2-yl-sulfanyl)-butyric acid;

2(R)-[4-(4-Fluoro-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-yl sulfanyl)-butyric acid, hydroxyamide;

3(R)-N-Hydroxy-4-(4-((pyridin-4-yl)methyl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

1-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-4-(1-methyl-1H-imidazole-4-sulfonyl)-piperazine-2-carboxylic acid hydroxamide;

N-(2,2-Dimethyl-1S-methylcarbamoyl-propyl)-3R-[1-(4'-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

3-Carboxymethylsulfanyl-2-(4-(4-fluoro-phenoxy)-benzenesulfonylamino)-3-methyl-butyric acid;

2,2-Dimethyl-1-oxo-4-[4-(pyridin-4yloxy)-benzenesulfonyl]-1S14-thiomorpholine-3-carboxylic acid hydroamide;

1-[4-(Pyridin-2-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-(fur-3-yl)-phenoxy)-benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfanyl)-butyric acid;

2,2-Dimethyl-1-oxo-4-[4-(pyridin-4yloxy)-benzenesulfonyl]-1S14-thiomorpholine-3-carboxylic acid hydroamide;

{2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-2-hydroxycarbamoyl-1,1-dimethyl-ethylsulfanyl}-acetic acid tert-butyl ester;

1-[4-(Pyridin-4-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-Bromo-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfanyl)-butyric acid, hydroxyamide;

trans-2-(2-Biphenyl-4-yl-ethylsulfanyl)-cyclohexanecarboxylic acid hydroxyamide;

N-[1S-(1H-Imidazol-2-yl)-3-methyl-butyl]-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid formate;

N-Methyl-3-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succinamic acid;

N(4)-(2,2-Dimethyl-1S-hydroxymethyl-propyl)-N(1)-hydroxy-3R-[3-(4-pyridin-4-yl-phenyl)-pyrrol-1-yl]-succindiamide;

{2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-2-hydroxycarbamoyl-1,1-dimethyl-ethylsulfanyl}-acetic acid;

1-[4[(4-Fluoro-phenoxy)-benzenesulfonyl)]-3,3-dimethyl-5-oxo-piperazine-2-carboxylic acid hydroxyamide;

N-(4-[4-Bromophenoxy]-benzenesulfonylamino)-3-methyl-3-(1-benzyl-imidazole-2-yl-sulfanyl)-butyric acid;

3R-[3-(4′-Cyanobiphenyl-4-yl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-hydroxymethyl-propyl)-succinamic acid;

2-(R)-[4-(4-Iodophenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-2-yl-sulfanyl)-butyric acid;

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-hydroxymethyl-propyl)-succinamic acid;

2(R)-[4-(4-Iodo-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid, hydroxyamide;

2(R)-[4-(4-Nitrile-phenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid;

2-[4-(-Fluoro-phenoxy)-benzene sulfonylamino]-3,3-dimethyl-pent-4-enoic acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyric acid;

2-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-3-methyl-3-(5-methyl-isoazole-3-ylmethylsulfanyl)-butyric acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyramide;

2-[4-(4-Bromo-phenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-(5-methyl-isoxazole-3-ylmethylsulfanyl)-butyramide;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(carbomethoxyethylsulfanyl)-butyric acid;

1-[2-(Benzothiazol-2-ylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(hydroxyethylsulfanyl)-butyric acid;

[4-Methoxy-benzenesulfonylamino]-3-methyl-3-(pyridin-2-yl-sulfanyl)-butyric acid;

N-(4,4-Dimethyl-2-oxo-tetrahydro-furan-3S-yl)-3R-[1-(4'-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

2-[4-(4-Fluorophenoxy)-benzenesulfonylamino]-3-methyl-3-(amidoethylsulfanyl)-butyric acid;

[4-Methoxy-benzenesulfonylamino]-3-methyl-3-(pyridin-2-ylsulfanyl)-butyric acid;

2-[4-(4-Fluoro-phenoxy)-benzenesulfonylamino]-3,3-dimethyl-5-phenyl-pent-4-enoic acid;

5-[4-(4-Fluoro-phenoxy)-benzenesulfonyl]-4,5,6,7-tetrahydro-3H-imidazole[4,5,-c]pyridine-6-carboxylic acid hydroxyamide

2(R)-[4-(4-Methylphenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid;

3(S)-4-(4-((Pyrid-4-yl)oxy)benzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxylic acid;

1-[4-(Pyridin-4-ylsulfanyl)-piperidine-1-sulfanyl]-piperidine-2-carboxylic acid hydroxyamide;

N-[1-(1H-imidazol-2-yl)-3-methyl-butyl]-3-[1-(4'-cyanobiphenyl-4-yl)-1H-pyrrol-3-yl]-succinamic acid;

3R-{3-[(4-Cyano-phenyl)-acetyl]-pyrrol-1-yl}-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid;

1-[4-(4-Methoxy-phenylsulfamyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

3R-[3-(4-Cyano-phenyl)-pyrrol-1-yl]-N-(2,2-dimethyl-1S-methylcarbamoyl-propyl)-succinamic acid methyl ester;

2(R)-[4-(4-Methylphenoxy)benzenesulfonylamino]-3-methyl-3-(pyridi-n-yl-sulfonyl)butyric acid, hydroxyamide;

1-[4-(4-Methyl-phenylsulfamyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxamide;

4-(4-Methoxy-benzenesulfonyl)-2,2-dimethyl-thiomorpholine-3-carboxylic acid;

4-4(-Methoxy-benzenesulfonyl)-2,2-dimethyl-thiomorpholine-3-carboxylic acid hydroxyamide;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid hydroxyamide;

2(R)-[4-(4-bromo-phenoxy)benzenesulfoxylamino]-3-methyl-3-(pyridi-n-yl-sulfuroxide)butyric acid, hydroxyamide;

4-(4-Methoxy-bezensulfonyl)-2,2-dimethyl-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

2,2-Dimethyl-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]-thiomorpholin-3-ol;

4-[4-(4-Chloro-phenoxy)-benzenesulfonyl]-2,2-dimethoxy-1-oxo-thiomorpholine-3-carboxylic acid hydroxyamide;

2-(R)-3-Methyl-3-(pyridin-2-yl-sulfanyl)-[4-(4-trifluoromethylphenoxy)benzenesulfonylamino]-butyric acid;

3(R)-4-(4-(Pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-tetrahydro-2H-1,4-thiazine-3-carboxamide;

2R-3-Methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-oxy)-benzenesulfonylamino]-butyric acid;

2R-N-Hydroxy-3-methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-oxy)-benzenesulfonylamino]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-3-hydroxy-3-methyl-butyric acid;

3(S)-2,2-Dimethyl-4-[4-(pyridin-4-ylsulfanyl)-benzenesulfonyl]-thiomorpholine-3-carboxylic acid hydroxyamide;

2R-3-Methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-sulfanyl)-benzenesulfonylamino]-butyric acid;

2R-N-Hydroxy-3-methyl-3-[(5-methyl-isoxazol-3-yl)methylsulfanyl]-[4-(pyridin-4-yl-sulfanyl)-benzenesulfonylamino]-butyramide;

3,3-Dimethyl-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyric acid;

3,3-Dimethyl-N-hydroxy-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-N-hydroxy-3-methyl-3-[(1-methyl-imidazol-2-yl)methylsulfanyl]-butyramide;

2R-[4-(4-Bromophenoxy)-benzenesulfonylamino]-3-methyl-3-[(1-methyl-imidazol-2-yl)methylsulfanyl]-butyric acid;

N-Hydroxy-2-[(4-methylbenzenesulfonyl)amino]acetamide;

1-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

1-[4-(4-Imidazol-1-yl-phenylsulfanyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

2(R)-[4-(4-Chloro-benzoyl)-cyclohexanesulfonyl]-piperidine-1-carboxylic acid hydroxyamide;

1(R)-[4-(4-Chloro-benzoyl)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid amide;

1(R)-(4-Pyridin-2-yl-piperazine-1-sulfonyl)-piperidine-2-carboxylic acid hydroxyamide;

1(R)-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid;

1(R)-[4-(4-Imidazol-1-yl-phenoxy)-piperidine-1-sulfonyl]-piperidine-2-carboxylic acid hydroxyamide;

N-Hydroxy-3,3-dimethyl-2R-[4-(morpholine-4-carbonyl)piperidine-1-sulfonylamino]butyramide;

N-Hydroxy-3-methyl-3-(5-methyl-isoxazol-3-yl-methylsulfanyl)-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-sulfonylamino]-butyramide;

4-(4′-Chloro-biphenyl-4-yl)-2RS-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-oxo-butyric acid;

4-(4′-Chloro-biphenyl-4-yl)-2R-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-4-oxo-butyric acid;

N-Hydroxy-2R-[4-(4-imidazol-1-yl-phenoxy)-piperidine-1-sulfonylamino]-3,3-dimethyl-butyramide;

2R-[4-(4-Chloro-benzoyl)-piperazine-1-sulfonylamino]-N-hydroxy-3-methyl-3-methylsulfanyl-butyramide;

N-Hydroxy-3-methyl-3-methylsulfanyl-2R-[4-(pyridin-4-ylsulfanyl)-piperidine-1-sulfonylamino]-butyramide;

4-(Pyridin-4-yloxy)benzenesulfonic acid;

4-(Pyridin-4-yloxy)benzenesulfonyl chloride hydrochloride;

(3S)-2,2-Dimethyl-3-thiomorpholine carboxylic acid;

3(R)-N-Hydroxy-4-(4-(pyridin-4-yl)oxybenzenesulfonyl)-2,2-dimethyl-1,1-dioxo-tetrahydro-2H-1,4-thiazine-3-carboxamide;

1R-3S-2,2-Dimethyl-1-oxo-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]-1-thiomorpholine-3-carboxylic acid amide;

1S-3S-2,2-Dimethyl-1-oxo-4-[4-(pyridin-4-yloxy)-benzenesulfonyl]-1-thiomorpholine-3-carboxylic acid amide; and

4-[4-(1-Hydroxy-pyridin-4-yloxy)-benzenesulfonyl]-2,2-dimethyl-thiomorpholine-3-carboxylic acid amide.

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(54) Title: COADMINISTRATION OF ACAT AND MMP INHIBITORS FOR THE TREATMENT OF ATHEROSCLEROTIC LESIONS

(57) Abstract

This invention is the coadministration of ACAT and MMP inhibitors for the reduction of both the macrophage and smooth muscle cell component of atherosclerotic lesions, thus impairing the expansion of existing lesions and the development of new lesions and for the prevention of plaque rupture and the promotion of lesion regression in a mammal.

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INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/US 99/13948

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K45/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 491 172 A (LEE HELEN T ET AL) 13 February 1996 (1996-02-13) cited in the application column 6, line 13 - line 19 column 11, line 55 -column 22, line 67	30,31
A	WO 98 09934 A (BRIEN PATRICK MICHAEL O ;WARNER LAMBERT CO (US); PICARD JOSEPH ARM) 12 March 1998 (1998-03-12) abstract; claims	1-18, 32-36
A	WO 97 44315 A (WARNER LAMBERT CO) 27 November 1997 (1997-11-27) abstract; claims	1-18, 32-36

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
16 March 2000	24/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Leherte, C

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/US 99/13948

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 05868 A (WARNER LAMBERT CO ;KRAUSE BRIAN ROBERT (US)) 20 February 1997 (1997-02-20) abstract; claims	1-18, 32-36
A	WO 94 19330 A (WARNER LAMBERT CO) 1 September 1994 (1994-09-01) abstract; claims	1-18, 32-36

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/13948

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-18,32,34-36
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 1-18,32,34-36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 30-32, 34

Present claims 1-18, 33, 35 and 36 relate to a pharmaceutical composition defined (inter alia) by reference to desirable characteristics or properties, namely an ACAT inhibitor with a MMP inhibitor. The claims cover all combinations of compounds having those characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such combinations. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Moreover present claims 3-6, 9-13, 15, 16 and 18 relate to extremely large numbers of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed.

Present claims 19-23 and 25-29 refer to R1 or R2 in claim 14, claim, which only contains a well defined compound. As a consequence those claims lack clarity and are impossible to search. The same counts for claim 24 which refers to disubstitutions in a formula in claim 16, in which those substitutions are not mentioned.

In the present case, the claims so lack support, the application so lacks disclosure, and the lack of clarity is such as to render a meaningful search over the whole of the claimed scope impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the combination by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds explicitely mentioned in claims 30 and 31 (allthough those two claims refer to claim 14, which cites a completely different compound), the combinations in claims 32 and 34 (claims which are totally identical) with due regards to the general idea underlying the application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna al Application No
PCT/US 99/13948

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